THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—34TH YEAR. SYDNEY, SATURDAY, JANUARY 4, 1947. No. 1.

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THE AUSTRALASIAN ANOPHELINES AS VECTORS OF MALARIA.

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Introduction.

WE began the recent war in the Pacific with the information, derived from Heydon (1923)[11] and de Rook (quoted in Swellengrebel and Rodenwaldt, 1932[35]) that *Anopheles punctulatus* was an important malaria carrier in New Britain and New Guinea, and with a certain dark suspicion of *Anopheles annulipes* on the mainland. That information carried us a long way, but the war brought a flood of new work, which has added considerably to our knowledge, and given some degree of precision to what was previously conjectural. The time is opportune, therefore, to review what we know now of the transmission of malaria in this region. This can be done the more effectively because the monograph of Lee and Woodhill (1944)[17] has provided us with a firm taxonomic framework on which the experimental and observational data can be arrayed.

As the possibility of malaria spreading and becoming established in new areas on the mainland still seems to be a matter of some debate, brief consideration may be given to that subject also, for it is intimately bound up with the "vector qualities" of the species.

My claim to be the author of this paper rests rather on the fact that I was responsible for much of the pertinent work being carried out than that I undertook any great part of it myself. Those who did the work were the people in the field and in the laboratory, especially Dr. G. A. M. Heydon, who was allotted by the Commonwealth Health Department to investigate the Cairns epidemic, and cooperate in many other ways; Major M. J. Mackerras in charge of the transmission work of the Land Headquarters Medical Research Unit at Cairns; and Majors F. H. S. Roberts, D. O. Atherton and S. L. Allman; and Lieutenants P. J. O'Sullivan, T. H. Lemerle and S. V. Bayley. These and others named in appropriate places in the text contributed most largely to the studies of Anopheline behaviour, feeding preferences, and infection rates in the field. No acknowledgements would be complete without expression of my great indebtedness to Major F. N. Ratcliffe, not only on many personal grounds, but for the part he played so unobtrusively in fitting people to their tasks and in ensuring them the opportunities and means to carry them out. Without his help this paper (and indeed Lee and Woodhill's monograph) would have been woefully incomplete.

Finally, I would express my thanks to Dr. A. J. Nicholson, Chief of the Division of Economic Entomology, Council for Scientific and Industrial Research, for permitting the work to be written up while I was a full-time officer of the Council.

Distribution of Malaria.

The distribution of malaria in the Australasian region has been reviewed by Cilento (1924)[5] and Ford (1943)[8] and need only be described briefly here as a necessary background to the studies of transmission. The classification of endemicity used, with the type of transmission generally associated with the various grades, is set out in Table I. Cilento's map gives a good picture of the general situation.

North and east of Australia malaria is hyperendemic below about 2,000 to 3,000 feet elevation on all the main islands from the Moluccas to the New Hebrides, endemic and highly endemic in certain drier parts of the south coast of New Guinea (for example, Port Moresby, Merauke) and on some of the smaller islands, falls off and disappears between 3,000 and 6,000 feet elevation, and may be absent from a few of the smallest, more isolated islands. Generally, transmission is intense and usually perennial.

On the mainland of Australia the situation is entirely different. Malaria is maintained in a condition of smouldering hypoendemicity among the natives of the main river systems and wetter parts of the coasts of the Kimberley district of Western Australia, the Northern Territory, the Gulf country of Queensland, and Cape York Peninsula, with seasonal extensions inland and to part of the white population. Throughout these areas there is in addition a marked liability to epidemic outbreaks, usually following the introduction of *Plasmodium falciparum*, and associated with "heavy wet seasons followed by spells of warm, humid weather, along with some abnormal concentration of humans" (Kirkland, 1939[14]).

TABLE I.
Degrees of Endemicity.

Classification.	Spleen Rate of Population.	Transmission.
Hyperendemic ..	>50%	Intense, perennial or seasonal.
Highly endemic	26% to 50%	Moderate; usually seasonal.
Endemic ..	10% to 25%	Moderate to light; seasonal.
Hypoendemic ..	<10%	Slight, irregular, fluctuating.
Sporadic ..	0%	Rare, "accidental".

On the east coast of Queensland similar hypoendemic patches occur as far south as the Mulgrave valley or possibly Ingham (Cilento). Epidemics, differing from those of the Northern Territory in that they probably represent normal fluctuations of hypoendemic *Plasmodium vivax* malaria, have occurred several times at Cairns (Breinl and Taylor, 1918;[3] Heydon, 1942, unpublished), which was the only large urban centre of endemic malaria in Australia.

South of 19° south latitude in Queensland we enter the zone of rare sporadic malaria, which probably embraces all the rest of the country with a rainfall greater than about 30 inches *per annum*. In a few favourable centres there have been groups of cases, as at Selheim, Ogmore and Canungra; for the rest, only individual cases have been recorded. It is interesting to note that only a very few doubtful cases have been observed at Townsville, which lies close to the endemic areas.

On the basis of the then existing knowledge Australia was divided for purposes of service administration and control during the war into the following broad zones, which illustrate very well the risks that were believed to be involved.

Malarious areas comprise New Guinea and the S.W. Pacific Area islands lying west of 170° E. long., and north of 20° S. lat., with the exception of Thursday Island and Horn Island.

Potentially malarious areas . . . comprise the following sections of the Australian mainland:

Northern Territory: The area north of 17° S. lat. (This parallel of latitude crosses the N.-S. road at a point between Daly Waters and Newcastle Waters.)

Western Australia: The area north of 19° S. lat., but excluding the coastal strip up to and including Broome.

Queensland: The area north of 19° S. lat., but excluding Horn Island and Thursday Island and that portion of the Atherton Plateau lying above 2,000 feet elevation.

Non-malarious areas are those portions of the mainland of Australia and the associated islands not specifically defined as either malarious or potentially malarious.

The Characteristics of Vector Species.

There is a striking apparent difference between the transmission of malaria, as it is observed in the field, and experimental transmission in the laboratory. In the field malaria would seem to be amongst the easiest of infections to transmit, amongst the most difficult to avoid. The steepness and severity of the epidemic wave, whether in troops (Fairley, 1946[7]) or unprotected civil populations (Soper and Wilson, 1943[30]), the universality of infection in hyperendemic communities, the difficulties of control, and the way in which *Plasmodium vivax* can maintain its hold under apparently most unfavourable conditions (Hackett, 1937[10]) all suggest ease and smoothness of transmission and a high degree of adaptation of the parasite to its means of dispersal.

Laboratory experience is precisely the opposite. The frequency of "bad" gametocyte carriers, the difficulties in ensuring survival of the mosquitoes and sometimes in inducing them to bite, the very large numbers of mosquitoes which must be handled, fed and nursed in order to produce even a moderate number of experimental infections, all point to transmission as being the most hazardous period in the life of the parasite, and to a slender, easily broken thread of survival.

Actually the anomaly is only apparent, for there are numerous observations to prove that these difficulties in transmission do exist in the field as well as in the laboratory. Where the laboratory studies have been particularly valuable has been to show them up in strong relief and to demonstrate that an Anopheline must possess special properties in order to be a successful vector of malaria. This point was well illustrated at Cairns (M. J. Mackerras and Roberts, unpublished). Considerable difficulty was being experienced in maintaining sufficient stocks of infected mosquitoes for the work, while the local *Anopheles punctulatus farauti* and *Anopheles annulipes* were being used. The introduction of *Anopheles punctulatus punctulatus*, with its great avidity for human blood and longevity in the laboratory, revolutionized the work. Infections on the scale required (Fairley, 1945,[6] 1946[7]) were still not easy to provide, but they became vastly less difficult than they had been, while the scope and magnitude of the work were actually expanded.

It is not to be inferred that behaviour in the laboratory means equivalent behaviour in the field, so far as the individual species are concerned, but the principle is universal, and it is with the principle that we are concerned here.

These observations are not new. James (1926)[13] from his laboratory experience was profoundly impressed with the same point of view, and even went so far as to conclude that the only Anophelines which could transmit malaria successfully in nature were certain aberrant individuals which led an abnormal life. Actually, possession of the combination of qualities which makes for success in transmission is not an individual but a specific or racial characteristic, and this is the basis of the firmly established principle of species sanitation. These qualities, propounded by Swellengrebel, Schüffner and Swellengrebel de Graaf (1919),[29] and confirmed and slightly modified by many later workers, are susceptibility to infection, abundance, association with man, avidity for human blood (anthropophilism), longevity.

Of the five, laboratory and field experience would point to anthropophilism as the most important. However, what a species may lack in one quality it may make up by a superabundance of another. Thus the highly anthropophilous *Anopheles fluviatilis* is a successful vector in parts of India at a lower abundance than the feebly anthropophilous *Anopheles culicifacies*, which must be present in high density to be an effective transmitter (Russell and Mohan, 1939[20]). It is of considerable interest to examine the Australasian Anophelines in relation to these qualities, for it is to be emphasized that it is on them that the present and future distribution of malaria in the region primarily depends, unless human population densities change very radically.

Susceptibility to Infection.

The need for susceptibility to infection as a basic property is obvious: if a species is insusceptible, it cannot transmit the parasite. But the converse by no means follows, and susceptibility to infection cannot be taken to indicate that a species is a vector in nature (Green and Gater, 1931[9]). *Anopheles stigmaticus*, mentioned below, is a case in point. Moreover, the technical difficulties in studying susceptibility, especially relative susceptibility, are much greater than was appreciated in early work on the subject. It is easy to obtain infection rates varying from 0% to 100% in the same species of Anopheline

infected by the same strain of parasite under different conditions, so that it is impossible to compare the susceptibility of different species to infection, unless they have been fed simultaneously on the same gametocyte carriers and the numbers of replications and of dissections have been statistically adequate. It is even more difficult to decide whether a given Anopheline is a better host for one species of parasite than another, and the published evidence on this head, especially that relating to *Plasmodium malariæ*, is not at all convincing. The need for a well-known, susceptible species to be included as a standard "yardstick" in all experiments is very apparent (Russell and Mohan, 1939[20]).

In Australasia there is such a "yardstick" in *Anopheles punctulatus punctulatus*, but most of the comparative work was done before it was stabilized. Nevertheless, there is sufficient evidence to show that many species (all, in fact, so far examined) are susceptible to infection (Table II),

TABLE II.

Experimental Infections of Anophelines.

Species.	Parasites.	Author.
Anopheles punctulatus punctulatus Don.	*Plasmodium falciparum.*	Heydon (1923).[11]
	Plasmodium falciparum, Plasmodium vivax, Plasmodium malariæ.	M. J. Mackerras and Roberts.
Anopheles punctulatus farauti Lav.	*Plasmodium falciparum, Plasmodium vivax.*	Heydon (1923),[11] Roberts (1943),[21] M. J. Mackerras and Roberts.
Anopheles annulipes Walk.	*Plasmodium falciparum, Plasmodium vivax.*	Roberts (1943),[21] M. J. Mackerras and Roberts.
	Plasmodium vivax.	Heydon (1935, unpublished), Bentley *et alii* (1936).[1]
Anopheles amictus amictus Edw.	*Plasmodium falciparum, Plasmodium vivax.*	M. J. Mackerras and Roberts.
Anopheles amictus hilli L. & W.	*Plasmodium falciparum.**	M. J. Mackerras and Roberts.
Anopheles meraukensis Venh.	*Plasmodium vivax.**	M. J. Mackerras and Roberts.
Anopheles longirostris Brug.	*Plasmodium falciparum, Plasmodium vivax.**	M. J. Mackerras and Roberts.
Anopheles subpictus Grassl.	*Plasmodium falciparum, Plasmodium vivax.*	Soesilo in Java (in Christophers, 1933).[4]
Anopheles bancrofti bancrofti Giles.	*Plasmodium vivax.*	Heydon (1942, unpublished).
	Plasmodium falciparum, Plasmodium vivax.	M. J. Mackerras and Roberts.
Anopheles stigmaticus Sk.	*Plasmodium falciparum, Plasmodium vivax.*	M. J. Mackerras and Roberts.

* These infections were tested to oocyst stage only; those not marked by an asterisk are for sporozoite infections in glands.

while comparative feedings (Roberts, 1943[21]; M. J. Mackerras and Roberts, unpublished) do not indicate any substantial differences between the commoner species. It would appear, therefore, that, unlike the other qualities, susceptibility to infection is a general rather than a specific or racial character in this region, and that the reasons for differences in epidemiological importance between species must be sought in those other qualities.

Abundance.

The quality of abundance, like the previous one, is basic. Only a proportion of the Anopheline population (depending on the degree of anthropophilism) will encounter man, only some of these will happen to feed on "good" gametocyte carriers, a fraction of them will survive to develop gland infections, and a proportion of the survivors will meet susceptible human hosts. Clearly, the general Anopheline population must normally be dense for there to be enough survivors to maintain a significant level of transmission in the community.

Density as a quality is, however, subject to two limitations. In the first place, its measurement is usually so much a matter of guesswork that it can be assessed only in a broad general way; and secondly, like susceptibility, abundance does not necessarily imply that a species is a good vector. *Anopheles bancrofti* at Cairns and *Anopheles longirostris* in some parts of New Guinea are examples of abundant species which were not transmitting malaria, although both human and parasite populations were adequate. In addition, even general assessment needs to be done expertly. An important species with cryptic habits may easily be overlooked, and we have had the experience of intense epidemics due to *Anopheles punctulatus* when even medical officers had not seen a single adult Anopheline in the area.

In spite of these limitations, this quality is a valuable one, for it immediately enables us to eliminate "zoological curiosities" and so reduce our list of regional species to a relatively small number, which could be significant vectors, and so merit closer attention. These more abundant species may be conveniently divided into those which are widespread and might be dangerous over broad sections of the region, and those which are numerous only in some localities and perhaps at particular times of the year (Table III).

TABLE III.

The Abundant Australasian Anophelines.

Widespread.	Local.
Anopheles punctulatus farauti Lav.	*Anopheles amictus hilli* W. & L.
Anopheles punctulatus punctulatus Don.	*Anopheles amictus amictus* Edw.
Anopheles annulipes Walk.	*Anopheles meraukensis* Venh.
Anopheles bancrofti bancrofti Giles.	*Anopheles novaguinensis* Venh.
	Anopheles subpictus Grassl.

Association with Man.

This leads us from the broader, more basic qualities to those more special ones which determine whether or not a particular Anopheline is dangerous. It lacks the precision of a study of host preferences, with which it is closely linked, but gives valuable preliminary information, and is a useful guide when for any reason blood spots for precipitin tests cannot be collected. Like abundance, it can only be discussed in general terms.

Temperate climate Anophelines (for example, the *Anopheles maculipennis* complex) are often domestic and tend to live in the sheds and habitations of man, whether they have a preference for human blood or not. Shelter seems to be the important factor. Tropical Anophelines, on the other hand, with comparatively few exceptions (of which *Anopheles gambiæ* is the most notable) shelter out of doors and only visit habitations to feed. The Australasian species are all predominantly outdoor dwellers, and excellent work was done by Atherton and Lemerle and by Roberts and O'Sullivan (unpublished army reports) in elucidating this problem in New Guinea and North Queensland. The normal resting places in the bush of *Anopheles punctulatus farauti*, *Anopheles punctulatus punctulatus*, *Anopheles amictus hilli* and *Anopheles longirostris* are now fairly well known, and Belkin, Knight and Rozeboom (1945)[2] have described those of the *lungæ* complex in the Solomon Islands. It is interesting to note that on the mainland *Anopheles annulipes* must be particularly cryptic, for its actual resting places are still obscure in spite of a fair search, although many entomologists know the sort of situation in which adults may be most readily collected by using themselves as bait.

The possibilities of associating with man have differed markedly between New Guinea and Australia since Pleistocene times. In New Guinea there has been a dense native population, and the mosquitoes have had every opportunity to become associated with it. It is probably significant in this connexion that Atherton and Lemerle found a steadily decreasing density of *Anopheles punctulatus farauti* with increasing distance from a native village, 80% of those collected in the bush being within 300 yards of the village. Roberts found the same tendency of *Anopheles punctulatus farauti* to concentrate near settlement at Cairns, in striking contrast to *Anopheles amictus hilli*, which concentrated at its breeding grounds. Bayley later observed a similar phenomenon with *Anopheles punctulatus punctulatus* at Milne Bay. Indeed, it is a commonplace experience in New Guinea that one cannot collect adult *Anopheles punc-*

tulatus of either subspecies at any great distance from concentrations of human beings, and one's own observations would suggest that natives are more attractive than whites, a point previously noted by Roberts (unpublished army report).

In Australia, by contrast, as particularly exemplified by the Northern Territory, the Anopheline population has enormously preponderated over the human, and no one can have been assailed by swarms of hungry Anophelines in almost uninhabited swampy parts of the Territory without being convinced that they must normally have used other animals than man as their main source of food. These remarks apply particularly to *Anopheles bancrofti* (over most of its range) and *Anopheles annulipes*, which bite vigorously when presented with human blood, but never seem to seek it out by preference and rarely show any signs of concentration in relation to human settlement. They are also true for *Anopheles amictus amictus* and *Anopheles amictus hilli*, and apparently for *Anopheles meraukensis* and *Anopheles novaguinensis*, which are abundant at times in parts of northern Australia.

Thus one would conclude that *Anopheles punctulatus* (in its various forms) in New Guinea does tend to associate with man, but that the other New Guinea species[1] and the mainland Anophelines do not.

Two special cases may be mentioned. By reason of its preference for breeding in small muddy collections of water and the remarkable ability of its larvæ to thrive in shallow waters strongly heated by the sun, *Anopheles punctulatus punctulatus* quickly occupies man-made breeding grounds, such as footprints, wheel-ruts, roadside gutters, borrowpits and the like. This quality makes it by far the most dangerous Anopheline (though the most easily controlled) in military operations in most parts of New Guinea. *Anopheles punctulatus farauti* sometimes shows the same tendency, but not to the same degree, and usually in the outlying parts of its range, where *Anopheles punctulatus punctulatus* is rare or absent.

The second case concerns *Anopheles subpictus*. Normally this species seems to be rather indifferent to man, but Bayley (unpublished army report) found a local population at Wedau (New Guinea) which rested throughout the day in large numbers in native huts in a manner reminiscent of some records of *Anopheles sundaicus*.

Avidity for Human Blood.

Field experience in many malarious countries would place avidity for human blood as the most important single factor of all; and theory is very much in accord with practice, for a specific feeder is far more likely to be an efficient vector than one which picks up parasites by chance and dissipates many of them among insusceptible recipients. For this reason precise studies of blood feeds form an important part of malariological investigations in other countries, though, unfortunately, they were not undertaken in Australia prior to the recent war.

Three lines of inquiry may provide information about this quality: precipitin tests of blood spots made from recently engorged Anophelines collected in the field; observations of feeding habits in nature; and a study of feeding behaviour in the laboratory. The first is by far the most reliable, but the others are not to be despised as subsidiary lines of inquiry.

Precipitin tests have been made by Dr. G. A. M. Heydon, of the School of Public Health and Tropical Medicine, on material collected by several army entomologists in the field. For these tests to have real significance it is essential, as Heydon has pointed out, that they be made on a truly representative cross-section of the mosquito population. This has not always been possible under service conditions. In particular, examination of mosquitoes caught in dwellings, though legitimate enough in some countries, is open to grave suspicion in this region, where the Anophelines generally enter dwellings to feed rather than to rest, so that there is a high *a priori* probability that any found engorged indoors will contain human blood. Thus the fact that 85% of 95 *Anopheles bancrofti* and 82% of 62 *Anopheles punctulatus farauti* from Merauke (Mandelson) contained human blood can be given little weight, for they were all collected inside occupied huts. On the other hand, there may be significance in the observation that 95 of 96 *Anopheles subpictus* from Wedau referred to above (Bayley) were found to contain human blood, though this would need confirmation by more detailed population studies.

The tests made on Anophelines collected in their natural resting places, on the other hand, are extremely suggestive, and these are set out in Table IV. Only those giving a reaction are included, for Heydon reported that most of the "negatives" were from poor spots, which could not be expected to react even with homologous antisera.

The numbers are not large, but the differences are very striking, particularly between the *Anopheles punctulatus farauti* from Lalapipi and the second series of *Anopheles punctulatus punctulatus* from Milne Bay, which were collected in a similar way around native villages. Further series from different localities would be desirable before definite conclusions are drawn, but the inference in the meantime remains, and nothing is known from observations of behaviour in the field elsewhere to negative it, except an indication in Belkin *et alii* (1945)[(1)] that *Anopheles punctulatus punctulatus* loses its avidity for human blood near the extreme eastern margin of its range.

Too few spots have so far been examined from *Anopheles annulipes* to be worth recording, no doubt primarily owing to the difficulty noted above in collecting engorged adults in their natural haunts. We therefore know nothing of the feeding preferences of this species, other than that it accepts human blood freely when it is offered. The same is true in general of field observations on feeding—they tell us that a given vertebrate species is not despised as a source of blood, but do not usually indicate what is preferred. Negative observations of this kind are often more useful than positive ones. *Anopheles bancrofti* in the Northern Territory is one of the most vicious biters and greediest feeders of all Australian mosquitoes. The Cairns race is morphologically indistinguishable from it (Lee and Woodhill, 1944, page 117[(17)]) and is present in large numbers in the district, but it scarcely ever attacks man, although it can be induced to take human blood fairly readily in the laboratory. Large populations of *Anopheles longirostris* have been observed to be almost completely indifferent to human blood in the field (Atherton), the explanation subsequently being found in Heydon's demon-

[1] *Anopheles bancrofti* may possibly be an exception in western New Guinea.

TABLE IV.

Blood Feeds of Australasian Anophelines (Heydon).

Species.	Locality and Collector.	Number Reacting.	Percentage with Human Blood.	Remarks.
Anopheles punctulatus punctulatus ..	Milne Bay (Aberdeen and Brasher).	37	95	Others *plus* dog, *plus* cat.
	Milne Bay (Bayley).	50	94	Others *plus* dog.
Anopheles punctulatus farauti ..	Lalapipi (Atherton and Lemerle).	88	19	Others *plus* dog (47%), *plus* pig (33%), *plus* cat (1%).
	Cairns (Roberts and O'Sullivan).	81	9	Others *plus* fowl (37%), *plus* ruminant (26%), *plus* horse (22%), *plus* dog (6%).
Anopheles longirostris	Bulldog (Langdon and Lemerle) } Milne Bay (Aberdeen) }	104	1	93% *plus Trichosurus*.

stration of its strong preference for marsupial blood (Table IV). Belkin *et alii* (1945)[1] observed a similar indifference to man in the related *Anopheles lungæ* and found that 70% of specimens with recognizable blood cells in their stomachs had fed on animals with nucleated red cells, though the remainder had attacked mammals.

The third source of information, that from laboratory observations, is, so far as it goes, unequivocal. *Anopheles punctulatus punctulatus* fed more readily than any other species in the laboratory (except an occasional batch of *Anopheles punctulatus farauti*), and this fact, as indicated earlier, had a profound effect on the whole course of the work (M. J. Mackerras, personal communication). *Anopheles punctulatus farauti* was generally slow to feed and had to be encouraged with hot, moist towels, while *Anopheles annulipes* and *Anopheles amictus amictus* were still more difficult, though Roberts (1943)[21] had earlier had less trouble with *Anopheles annulipes* than with *Anopheles punctulatus farauti*. Apart from these common species, which were known to attack man in the field, three species, *Bironella gracilis* Theo., *Anopheles stigmaticus* Sk., and *Anopheles longirostris* Brug, which rarely or never feed on man in nature, were induced to do so in the laboratory.

When all the evidence is taken together, the conclusion seems indicated that *Anopheles punctulatus punctulatus* (at least the Milne Bay population) is strongly anthropophilic, *Anopheles punctulatus farauti* associates with man and his domestic animals, but has no particular feeding preferences between them, and a few species strongly prefer other animals. The evidence concerning *Anopheles annulipes* and *Anopheles bancrofti* is insufficient, but the former at any rate has no preference for human blood. If it had, the investigations of the past three years would certainly have demonstrated it.

Longevity.

Nothing is known of survival rates and duration of life of the Australasian Anophelines in nature, the only available information being from laboratory stocks at Cairns kept under as favourable conditions as possible (M. J. Mackerras and Roberts). Data for four common species are shown in Table V, the seventeen-day period being chosen because it was convenient for transmitting experimental infections, and the months because they were favourable for the particular species.

It cannot be suggested whether these figures mean anything in relation to natural survival rates, but it is rather interesting that *Anopheles punctulatus punctulatus* retains its preeminence in this as in other respects in which it has been tested. Large-scale observations on stained Anophelines liberated near a compact native settlement would be needed to test the matter properly. They would be laborious, but well worth undertaking, for the natural "expectation of life" of the Anophelines is fundamental in epidemiology and is an almost unknown quantity anywhere in the world.

TABLE V.
Survival of Anophelines at Cairns.

Species.	Month.	Percentage Surviving to Seventeen Days.
Anopheles punctulatus punctulatus	October.	53
Anopheles annulipes	July-August.	38
Anopheles punctulatus farauti ..	July.	23
Anopheles amictus amictus ..	October.	1

Natural Infection Rates.

The final proof that an Anopheline transmits malaria in nature is to find it infected in the field. If one can then associate its sporozoite rate with an accurately determined biting rate, the intensity of transmission, and consequently the local importance of the species at the time, can be assessed. As pointed out elsewhere (Mackerras and Aberdeen, 1946[19]), this is difficult with the Australasian species, so it is usually necessary to rely on an analysis of the surrounding circumstances for guidance in interpreting the infection rates found. Of these, relationship to an epidemic wave, concurrent transmission by another species, and season are probably the most important.

The natural infections recorded in Australasian Anophelines are listed in Table VI, only a few Dutch records from the western edge of the region being omitted. These are noted in Lee and Woodhill (1944)[17] and mainly concern species which belong more properly to the Oriental region.

The first point of interest is that the majority of the records are for *Anopheles punctulatus*, which is a reflection of its abundance where malaria was being transmitted. Secondly, the three other species listed were all associated

TABLE VI.[1,2,3]
Natural Infections in Australasian Anophelines.

Species.	Locality.	Number Dissected.	Oocyst Rate *per Centum*.	Sporozoite Rate *per Centum*.	Remarks.
Anopheles punctulatus punctulatus Don.	Milne Bay.	61	11·0	8·0	In hyperendemic native villages (Aberdeen).
Anopheles punctulatus farauti Lav.	Wewak.	200	3·5	2·0	In hyperendemic native village (Mackerras and Aberdeen, 1946).[19]
	Wewak.	155	0	0·6	In troop encampments early in control period, June (O'Sullivan).
	Wewak.	320	0·3	0	In troop encampments, control established, July (Aberdeen).
	Wewak.	721	0	0	As above, August-September.
	Lalapipi.	500	1·2	0	In native village (Atherton and Lemerle).
	Lalapipi.	1,737	0	0·06	Same village (Roberts and O'Sullivan).
	Cairns.	1,535	—	0·65	In civilian epidemic (Heydon).
Anopheles punctulatus (mixed races)	Tanah Merah, November.	82	4·9	—	In early and later stages of epidemic in Malay settlers (de Rook, in Swellengrebel and Rodenwaldt, 1932).[22]
	December-January.	125	11·0	—	
	Pioniersbiwak.	448	2·7	—	In native community (de Rook, in Swellengrebel and Rodenwaldt, 1932).[22]
	Rabaul.	125	6·2	6·4	In native houses (Heydon, 1923).[11]
	Rabaul.	101	0	0	In white quarters (Heydon, 1923).[11]
	Ramu Valley.	330	1·8	1·8	In declining stages of epidemic in troops (Atherton and Lemerle).
	Lae.	81	1·2	0	In controlled native village (Aberdeen).
Anopheles subpictus Grassi ..	Lalapipi.	263	0·4	0	In native village (Roberts and O'Sullivan).
Anopheles amictus hilli W. & L...	Cairns.	79	0	1·3	In civilian epidemic due to *Anopheles punctulatus farauti* (Roberts).
Anopheles bancrofti Giles	Tanah Merah.	438	4·3	—	In epidemic due to *Anopheles punctulatus* (de Rook, in Swellengrebel and Rodenwaldt, 1932).[22]
	Cairns.	74	0	0	(Heydon.)

[1] A substantial part of this table has already been used by Lee and Woodhill (1944, Table XIV).
[2] The Dutch records for *Anopheles punctulatus* are included among the mixed races, as their descriptions show that they included many intermediates in each subspecies.
[3] In Dutch work, "infection rate" has usually meant oocyst rate, and the sporozoite rate was not determined. Their records are therefore included under oocyst rates here, although not originally stated to be so.

with *Anopheles punctulatus—Anopheles bancrofti* and *Anopheles amictus hilli*, with epidemics primarily due to *Anopheles punctulatus* and *Anopheles subpictus*, with endemic transmission by the same species. Thirdly, the absence of *Anopheles annulipes* is notable. In spite of constant vigilance, no opportunity arose during the war to dissect this species in circumstances which would offer the remotest hope of obtaining an infection rate. One small outbreak of *Plasmodium vivax* malaria at Selheim in North Queensland was almost certainly due to *Anopheles annulipes*, but it was so short-lived that it was over before an observer with a microscope could reach the spot.

The records for *Anopheles punctulatus* merit a little further consideration. Three are from epidemics—during the development of the epidemic wave at Tanah Merah, during its decline in the Ramu Valley, and in the midst of what would be, by New Guinea standards, a relatively mild flare-up of *Plasmodium vivax* malaria at Cairns. Both Lalapipi groups require the reservation that the dissections were made in the dry season, when the expectation of life of the Anophelines was relatively low (Atherton), and the picture might have been quite different if observations could have been made in the wet season. The community was a hyperendemic one and the abundance of *Anopheles punctulatus farauti* enormous, probably greater than was encountered anywhere else in the islands. These records and parasite surveys made by the 3rd United States Medical Laboratory (unpublished United States army reports), indicate that some transmission was going on, even in the dry season, no doubt by sheer weight of numbers, like *Anopheles culicifacies* in parts of India (compare Russell and Mohan, 1939[23]). The remaining records (Milne Bay, Pioniersbiwak, the first Wewak set, and Rabaul) are the most reliable, for they are all from fairly static, hyperendemic conditions and they clearly indicate that *Anopheles punctulatus* is a really efficient vector, comparable with the recognized dangerous species of other parts of the world.

Finally, the effect of Anopheline control is shown by the later Wewak figures (Mackerras, 1946[18]) and probably also by Heydon's records from Rabaul and those from Lae. We have, unfortunately, no strictly comparable records of sporozoite rates for Wewak or the Lae area before control began, but the previous incidence of clinical malaria for the one and a comparison with similar hyperendemic villages for the other are certainly suggestive.

Discussion.

Taking all the facts into consideration, the nine Anophelines listed in Table III may be graded in the following descending scale of importance as vectors of malaria:

Proven dangerous vectors:

Anopheles punctulatus punctulatus Don.
Anopheles punctulatus farauti Lav.

Potential vectors under locally favourable conditions:

Anopheles annulipes Walk.
Anopheles bancrofti bancrofti Giles.
Anopheles subpictus Grassi.
Anopheles amictus hilli W. & L.
Anopheles amictus amictus Edw.

Unknown, but at most locally significant:

Anopheles meraukensis Venh.
Anopheles novaguinensis Venh.

All other species may safely be excluded from any broad consideration of the region. The gradation, however, cannot be accepted without further discussion, for it has two weaknesses: it passes too summarily over the races of *Anopheles punctulatus;* and the sequence under the second and third headings will remain unproven until the vectors on the mainland, and particularly those of epidemic malaria in the Northern Territory, have been determined more fully. It therefore remains to consider these two points, and also the probable future distribution of the disease in this country.

The Races of Anopheles Punctulatus.

There is no question of the importance of the species *punctulatus* in the wide sense. In all its forms it is dangerous, and it was controlled wherever it was met. In this connexion, it is interesting to note that Lieutenant-Colonel J. C. English, who directed malaria control operations in Borneo after very extensive experience in New Guinea, stated (personal communication) that none of the other species he encountered, including *Anopheles sundaicus*, was as great a worry to the malariologist as *Anopheles punctulatus*. But *Anopheles punctulatus* is not a homogeneous species. Like many other Anophelines, it is in a state of evolutionary flux, with numerous local populations, each differing a little from the others (Woodhill, 1946[27]), and with two (or three) main races. Those clearly recognized are *Anopheles punctulatus punctulatus* Don. and *Anopheles punctulatus farauti* Lav. (= *moluccensis* Sw. and Sw. de G.; Knight and Farner, 1944[15]). The third gave uniform progeny in the Solomons, and was regarded by the American workers as distinct under the name *koliensis* Owen (Owen, 1945;[20] Rozeboom and Knight, 1946[22]); but produced very variable progeny at Salamaua, leading Woodhill (1946)[27] to believe that it was a hybird. These races and local populations differ not only in morphology, but in behaviour, so it is of some practical use to examine their relative capabilities as vectors.

Anopheles punctulatus punctulatus, as represented by the Milne Bay population, stands out as preeminent in every characteristic examined in the field and the laboratory, and it was associated with a most vicious epidemic of malaria in 1942. We would not, however, be on such safe ground in concluding that it behaves similarly everywhere throughout its range. Its predilection for small, man-made breeding grounds certainly remained constant in New Guinea, and it was not observed to change in other respects, but it was rarely given another chance to show its full potentialities and its study was confused in several areas, for example in the Ramu Valley, by the presence of numerous intermediates. In parts of New Britain and the Solomon Islands it was less numerous than in New Guinea, and Belkin *et alii* (1945)[1] considered that it showed little avidity for human blood near the eastern limits of its range.

Anopheles punctulatus farauti, on the other hand, was ubiquitous and fairly constant in behaviour over a wide area from Cairns to northern New Guinea and eastwards to Bougainville. Its "vector qualities" are not outstanding, but it was dangerous for two reasons: its populations were usually high in undisturbed coastal areas, and, on account of its more varied and obscure breeding grounds, it was more difficult to control than *Anopheles punctulatus punctulatus*. Indeed, the normal epidemiological sequence,[1] where both races occurred, would seem to have been early transmission from natives to troops by *farauti*, the developed epidemic wave associated with an enormous increase in *punctulatus*, and an obstinate residue of transmission by *farauti* left after control was established. Nevertheless *farauti* alone could be associated with epidemic malaria, but by reason of its abundance rather than its other qualities, and in circumstances in which *punctulatus* could not displace it as the primary vector; the American experience at Guadalcanal, quite as bitter as ours at Milne Bay, was probably the outstanding example.

The intermediate form is confusing, behaving in some respects liks *punctulatus* and in others like *farauti*, and apparently differing in behaviour in different areas. Thus Belkin *et alii* (1945)[1] in the Solomons and Atherton (unpublished) in the Ramu Valley describe behaviour like that of *punctulatus*, and the latter recorded a substantial infection rate (Table VI), while Woodhill's observations at Salamaua would tend to associate it rather with *farauti*. Biologically, it is worthy of careful investigation, but in the meantime one feels that the weight of evidence rests with Woodhill's (1946)[27] hypothesis that it is a hybrid.

The distribution of the races may be noted, for it influences the epidemiological situations likely to be encountered in different parts of the region.

Anopheles punctulatus farauti Lav. is widespread on all the larger and most of the smaller islands north of Australia from the Moluccas to the New Hebrides; it is abundant on the coast, disappears inland in many localities

[1] Only allowed to develop on a few occasions.

from 1,000 to 3,000 feet elevation, but is found again in the Mount Hagen, Chimbu, and Kainautu areas at an elevation of 5,000 to 6,000 feet (Bisset, in Lee, 1946[16]). On the mainland of Australia this race is common in east coastal Queensland as far south as Ingham and up to Kuranda (1,100 feet), and occurs as scattered populations in the Northern Territory from Darwin to the Katherine River and eastward to Groote Eylandt (Lee and Woodhill, 1944[17]); it is absent above 2,000 feet elevation (Roberts) and practically disappears south of the limits indicated, though there are a few southern records which require confirmation by more extensive collecting.

Anopheles punctulatus punctulatus Don. is more restricted in range than *Anopheles punctulatus farauti*, reaching its limit on Guadalcanal in the Solomon Islands and being absent from the New Hebrides and the mainland of Australia, except for an unconfirmed single record by Hill (1925)[19] at Boroloola in the Northern Territory. It is not usually abundant on the coast under normal conditions of native occupation, but is more numerous and often the only race present inland between 1,000 and 3,000 feet elevation (for example, at Bulldog, Yamil, Maprik, in New Guinea); only recorded once from higher country, at Chimbu (Bisset). Near its eastern limits it becomes decidedly rarer in Guadalcanal, Bougainville, and parts of New Britain than it is in New Guinea.

"Intermediates" (*koliensis* Owen) seem to occur wherever both races are present together, but have not been recorded in localities where either *punctulatus* or *farauti* have only been found alone. They were very rare at Milne Bay and rare at Wewak, but common on Guadalcanal (Owen, 1945[20]), Salamaua (Woodhill, 1946[27]), Aitape (Gilmour) and the Ramu Valley (Atherton).

The Vectors of the Mainland.

Two problems are presented here: the vectors of sporadic malaria in the south and those of endemic and epidemic malaria in the north. The first is relatively simple, because the only Anopheline present in sufficient numbers and with a sufficiently wide distribution is *Anopheles annulipes*. The same species, again because it was the only one found in the area, undoubtedly caused the small outbreaks at Selheim in North Queensland and Canungra near Mount Tamborine, and probably also that at Ogmore near St. Lawrence. It has already been emphasized that *Anopheles annulipes* shows no defined association with man, but it seems fairly clear that, if man is brought to the mosquito, for example, by placing a camp on the banks of a river where it is breeding in abundance, it will avail itself of the offered food and may transmit malaria if gametocyte carriers are presented to it. The great rapidity with which the Selheim outbreak was brought under control by improvised measures energetically applied (Sinnamon, unpublished), suggests that it provides a somewhat slender thread of continuity for the parasite.

The problem of coastal North Queensland is also clear. Heydon (unpublished) in the Cairns epidemic of 1942 established that the primary vector there was *Anopheles punctulatus farauti*, while Roberts (unpublished) showed that its practical southern limits were at Ingham, north of Townsville, and that it could not be found above 2,000 feet on the Atherton Tableland. His southern observations were confirmed by Perkins and by Pasfield (unpublished), who also could not find this species in careful and extensive searches for it at Townsville. The inference is strong, therefore, that *Anopheles punctulatus farauti* is the normal vector of this part of Queensland and that the limits of endemic malaria are determined by its distribution.

Hill (1925)[19] also recorded *Anopheles punctulatus farauti* in the Northern Territory, and the recent observations of army entomologists (Woodhill, Henry, Johnston and others) have considerably added to our knowledge of its distribution there. Again, it coincides fairly well with that of endemic malaria, and it is tempting to believe that it is the normal vector in the Territory as it is in east coastal Queensland. That conclusion, however, should be accepted with the greatest reserve, if at all. In the first place, owing largely to careful preventive measures (Johnston, unpublished), no significant outbreak of malaria occurred during the war and no opportunity arose, therefore, to determine a vector by dissection. Secondly, the abundance and behaviour of *Anopheles punctulatus farauti* in the Northern Territory were never such as to bring it under serious suspicion (Woodhill, unpublished), whereas several other species were extremely abundant at times and attacked man with great energy. Of these, the most conspicuous and consistent were *Anopheles annulipes* and *Anopheles bancrofti*, but *Anopheles amictus amictus*, *Anopheles amictus hilli*, and *Anopheles meraukensis* were sometimes numerous. The question must remain open until dissections can be made; but the history of epidemic malaria in the Territory bears a certain basic resemblance to the Selheim outbreak, and it may be suggested that probably any of the abundant species will serve, if human populations and parasites are presented to them in sufficient density. The self-limited character of past outbreaks is particularly suggestive in this connexion.

Future Distribution of Malaria.

Given the presence of parasites, the amount of malaria in a community depends basically on three factors, namely, the density of the human population, the "vector qualities" of the local Anophelines, and climate. The initial numbers of parasite carriers may be small or large, but final equilibrium depends on these three factors. The human population of Australia may change, but it shows no signs of the major redistribution which would be necessary to transform the epidemic risk that has been associated with mining ventures or constructional work in the north into the endemic malaria of a large, static population. The climate, too, is probably changing (for the worse), but so slowly as to be of no practical interest for the present generation.

As regards the Anophelines, there is strong reason to believe that all the species recorded from the mainland, including *Anopheles punctulatus farauti*, are native, in that they have been here from prehistoric times and that they have had ample time to become stabilized in both distribution and habits. Changes in them, therefore, cannot logically be expected to be rapid, though the possibility of gradual evolutionary increase in anthropophilism in response to an increasing density of human population certainly exists.

The essence of the position is that we are dealing with a relatively stable biological situation, established over a considerable period of time, and no sudden or drastic alteration is to be expected in it. Unusual concentrations of gametocyte carriers, as in returning troops, may produce minor fluctuations in the form of a crop of sporadic cases, or even a minor outbreak under specially favourable conditions, but the trend is always back to the norm and their effects should quickly disappear.

There is, however, one change that can be both sudden and drastic, and that is the introduction of a highly anthropophilous, efficient vector. The invasion of Brazil by *Anopheles gambiæ*, vividly described by Soper and Wilson (1943),[24] is an outstanding example. This is the real malarial danger facing the mainland of Australia, for there is at our doorstep in New Guinea a highly efficient vector in *Anopheles punctulatus punctulatus*, the introduction of which might be disastrous. It may be that if this subspecies came into Australia it would be restricted to the humid, tropical part of the north; but that would be bad enough and it would be worse than foolish to place any great reliance on such a likelihood. One may decry, with some justice, the expenditure of much energy on Anopheline control to prevent an occasional sporadic case,[1] but one feels that the real danger should be widely known and appreciated, as no doubt it is by the quarantine authorities.

Summary.

The "vector qualities" of the Australasian Anophelines are examined under the headings: susceptibility to infec-

[1] This statement in no way affects the position in the genuine endemic areas, such as Cairns, where there is every justification and responsibility to maintain the control established during the war.

tion; abundance; association with man; avidity for human blood; and longevity. The Milne Bay (New Guinea) population of *Anopheles punctulatus punctulatus* is pre-eminent in all qualities, while the species which are sufficiently abundant to merit consideration can be arranged in the following approximate descending order of importance:

Proven dangerous vectors:

Anopheles punctulatus punctulatus Don.
Anopheles punctulatus farauti Lav.

Potential vectors under locally favourable conditions:

Anopheles annulipes Walk.
Anopheles bancrofti bancrofti Giles.
Anopheles subpictus Grassi.
Anopheles amictus hilli W. & L.
Anopheles amictus amictus Edw.

Unknown, but at most locally significant:

Anopheles meraukensis Venh.
Anopheles novaguinensis Venh.

The primary vectors of New Guinea and the islands are the races of *Anopheles punctulatus*, the vector of north-eastern Queensland is *Anopheles punctulatus farauti*, while *Anopheles annulipes* is the presumptive vector of sporadic malaria in the south, and the vectors of the Northern Territory are still undetermined.

It is considered that there is no reason to expect any change in the distribution and amount of malaria on the mainland of Australia, unless a new vector is introduced. The possibility that *Anopheles punctulatus punctulatus* might be transported from the islands into the tropical parts of the mainland is a danger to be guarded against.

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INGUINAL HERNIA.

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THE repair of an inguinal hernia presents a complex problem, depending for its satisfactory solution on a detailed knowledge of the anatomy of each of the structures entering into the formation of the canal, including variations in type of the openings, the fascia and the muscular insertions, together with such defects in structure as occur from time to time, through which abdominal contents protrude, giving rise to a hernia.

The function and mode of action of each structure must be taken into consideration when one is planning the surgical procedure which is to be the most advantageous in each particular case.

A consideration of the varying types of herniæ will make it obvious that no one operation can possibly be expected to suffice for the repair of all inguinal herniæ. Broadly, the inguinal hernia is of two types: the indirect, coming through the internal ring, and travelling with the structures of the cord, and the direct, which bulges through the medial end of the canal as the result of a deficient posterior wall.

This distinction sounds simple and clear-cut. In practice, however, the clinical differentiation, in my experience, is often extremely difficult; an accurate diagnosis is possible only at operation, when the operative procedure must be varied according to the findings. This requires a good deal of judgement and experience, together with a versatile knowledge of the "tricks" and procedures available for closing unexpected or unanticipated structural deficiencies. Therefore, I believe it to be wrong that a hernial repair should be regarded as an operative exercise for a junior and inexperienced house surgeon, particularly so as the standard operative procedures of Bassini and Halsted are in my opinion based on inaccurate premises, and should be discarded.

Anatomy of Canal.

The Canal.

The inguinal canal, consisting of an anterior and posterior wall and a floor, opens laterally and above into the abdominal cavity at the internal ring, and medially and below, external to the abdominal wall at the external ring leading to the scrotum. Along the canal pass the cord structures.

Internal Ring.

The internal ring takes the form of a V-shaped band open above; the lateral limb is short and attached to the fascia over the transversus muscle, the medial limb is longer and attached to the transversus aponeurosis. The contraction of this muscle lifts the medial limb, narrowing

the opening and altering its direction, thus protecting it from intraabdominal pressure. The normal internal ring will just admit the tip of the index finger.

Posterior Wall.

Attached along the medial limb of the internal ring is the transversalis fascia, filling in the posterior wall between this and the conjoint tendon medially, to which it is also attached. Above, this fascia extends behind the transversus muscle, and below it gains attachment to the recurved portion of the inguinal ligament and to Thompson's ligament deep to this. The transversalis fascia is, in its outer half, comparatively thin, while medially, as Henle's ligament, it is thick, tough and resistant. With contraction of the abdominal muscles this fascia becomes tense.

Deficiencies of three types occur in this layer. First, the outer, thinner portion may be absent, a comparatively large gap being left, and it would appear that in these cases the internal ring becomes unduly large; this leads to the formation of the acquired type of indirect hernia. When an indirect sac is present with a narrow internal ring and a normal lateral transversalis fascia, it would be a reasonable presumption that the sac is congenital and is the unobliterated funicular process. Secondly, the medial transversalis fascia is fenestrated; usually one opening only it present slightly lateral to the conjoint tendon; the opening admits the tip of a finger, and through this comes a hernial sac. Thirdly, the whole fascia is deficient. Medial to this fascia, the posterior wall is formed by the conjoint tendon, which is inserted into the body of the pubis and the ileo-pectineal line for a varying distance. A narrow or absent insertion in this region is not infrequently associated with a deficient transversalis fascia, and leaves an inadequate posterior wall in an area where the anterior wall is normally absent—that is, opposite the external ring. With this deficiency occurs the large direct hernia. Fenestration of the conjoint tendon also occurs in a similar manner to that in the transversalis fascia, a narrow-necked hernial sac protruding. This type of hernia can be confusing if one is not familiar with the condition.

Anterior Wall.

The anterior wall of the canal is formed by the aponeurosis of the external oblique muscle. It consists of fibres running downwards and medially, separating below to form the two pillars of the external ring. The lower pillar is attached to the pubic tubercle, the upper pillar to the body of the pubis in front of and in conjunction with the rectus sheath crossing to the opposite side as the reflex inguinal ligament. Lateral to the apex of the external ring the parallel fibres of the external oblique aponeurosis are normally tied by interlacing transverse intercrural fibres. These may be few or absent, allowing the external ring to become stretched and enlarged, and giving weak anterior protection, accompanied by a bulging along the whole of the canal.

Floor.

Below, the external oblique aponeurosis is curled backwards to form the inguinal ligament, the gutter of which becomes the floor of the canal and serves the function of accommodating the structures lying within the canal and guarding them against pressure when the upper part of the canal is closed by contraction of the abdominal wall; which in effect leads to the lifting of the internal ring, tensing of the transversalis fascia and conjoint tendon, approximation of the two pillars of the external ring and an approximation of the anterior and posterior canal walls. The strength of the canal thus depends on narrow openings at either end, which are further narrowed by muscle action, combined with a strong anterior wall laterally and a strong posterior wall medially.

Operative Procedures.

The operation for a hernial repair should be based on two essentials: (i) to find and to deal suitably with the sac; (ii) to repair the structural deficiency; this repair should interfere as little as possible with the normal functioning of the structures involved, and should maintain the mechanics of the canal.

To repair a mechanical deficiency, this deficiency must first be found and accurately delineated. This, in other words, means isolation of the sac, whether it is of the glove-finger type as in indirect hernia, or the bulge, as in direct hernia. Yet it would appear that a common cause of recurrence is failure to find the sac; one is told from time to time, when asked to operate on a recurrent hernia, that at the original operation no sac was found, but a Bassini operation was carried out, and the hernia reappeared with the first cough. When one considers the operative details of hernial repair in the light of the two desiderata mentioned above (dealing with the sac and mechanical repair of the walls), one or both of these procedures may be necessary, according to the conditions found on exploration.

Indirect Herniæ.

In the congenital glove-finger type of hernia, in which the anatomy of the canal remains undisturbed and the internal ring remains normal, it is obviously sufficient only to remove the sac. To accomplish this, the sac can be readily isolated from the cord structures and picked up below the exteral ring. It is then invaginated into the abdomen, brought out through the abdominal wall and stitched to the external oblique fascia, just as one would turn the finger of a glove. Nothing further is required beyond closure of the skin wound. This simple procedure takes less than ten minutes to accomplish and gives satisfactory results with a minimum period of recumbency, incapacity and economic loss. Furthermore, in the event of a recurrence, the same procedure can be carried out on several occasions if the need should arise. I have had the opportunity of performing this operation three times on one person. On the first occasion a bilateral indirect hernia was operated upon; the hernia on the right side was large and irreducible, and contained adherent omentum. This right-sided hernia recurred in about twelve months, following the lifting of a bucket of sausage meat from the floor on the opposite side of a counter. At the second operation, an indirect sac was present and invagination was carried out. On this occasion the sac wall was thick, fleshy, œdematous and friable, and difficult to tie for this reason. This type of sac wall is unusual, and is always difficult to deal with owing to its friability. I can offer no satisfactory explanation for this peculiar condition of the sac, as I have seen it in herniæ of long standing and unrelated to trauma or strangulation. Nor does it appear to be a type of peritoneum peculiar to the subject; with the second recurrence in the above-mentioned case, which occurred about three months after the second operation and followed a fall while the patient was lifting a sheep from a hook in a freezing room, the peritoneum of the sac had returned to normal, and for the third time an invagination was carried out, with a satisfactory result.

In the next type or grade of indirect hernia, which may be congenital or acquired, the outer part of the transversalis fascia is deficient and there is an enlarged internal ring; a similar operation is frequently sufficient, and by firm traction on the invaginated sac one can make the transversalis fascia sufficiently tense to produce a satisfactory lateral posterior wall. This, however, is not always possible, and a further procedure, which will be mentioned later in the discussion on recurrent herniæ, may be necessary.

Combined with either or both the above types of indirect hernia there may be an unduly large external ring; this leads to inefficient anterior protection of the canal. This ring will then require repair, which can usually be carried out by stitching the pillars together, after a thorough cleansing by dissection and gauze polishing, to lower the apex of the ring. At times, however, a flap is necessary, similar to that used in the repair of a direct hernia.

Direct Herniæ.

Where the internal ring remains efficient, no indirect sac is present, and Hesselbach's ligament—that thickened lateral margin of the transversalis fascia running from

Thompson's ligament to the aponeurosis of the transversus muscle at the margin of the internal ring—remains in evidence, while that part of the transversalis fascia on the medial side disappears as an efficient member of the posterior canal wall. This state of affairs is often associated with an absence of the ileo-pectineal line insertion of the conjoint tendon, and thus an unprotected gap is left in the abdominal wall opposite the external ring, through which gap the abdominal contents bulge. This bulge is unlike the indirect sac, as it has no neck, being widest at its abdominal margin. Here the surgical problem becomes reversed, in that the anatomical defect, and not the sac, requires repair. Two methods are available. The first is closure of the gap in the posterior wall by replacement of the transversalis fascia. The second is the method I have found satisfactory, in which the anterior wall of the canal is prolonged downwards to bring the outlet of the external ring in front of the body of the pubis, which then becomes the posterior wall opposite the external ring. This is a comparatively simple procedure, effected by cutting a flap of rectus sheath, which is turned down and stitched to the polished lower pillar of the external ring, and the adjacent inguinal ligament. It is important that this flap should extend from lateral to the apex of the external ring to a point sufficiently medial to ensure that the pubis becomes the posterior wall of the canal. I make no attempt to deal with the direct sac, which is left untouched, and I have found that the results following this simple procedure are surprisingly good. The procedure to repair the posterior wall will be dealt with in the discussion of recurrent herniæ.

Herniæ through fenestrations in the transversalis fascia or conjoint tendon require ligation or oversewing of the neck of the sac, together with repair of the fenestration. For this I find it necessary to fill the gap with some form of flap; this can usually be obtained from the conjoint tendon. Stitching together of the margins of the opening does not appear to be sufficient or satisfactory. In my experience, this is followed by recurrence. This type of hernia, as mentioned before, is rare and confusing unless its occasional occurrence is borne in mind.

Comment.

These operative procedures interfere as little as possible with the normal anatomy, which is left intact. Fascial flaps are used to reinforce weakened or deficient areas. Particular care is taken to see that all flaps fit efficiently without tension. Age is not considered a bar to operation if the patient is well, and no attempt is made to keep the patients in bed after operation—in fact, they are encouraged to get up the next day, and few remain in bed longer than forty-eight hours. This is based on the belief that recumbency is unnecessary, and that normal activity leads to more efficient healing with a minimum of disuse atrophy of muscles. Return to work in approximately four weeks is encouraged.

Recurrent Herniæ.

In discussing recurrent herniæ, it is first necessary to comment on the operation which the recurrence follows.

Invagination Operation.

Recurrence following the invagination operation, mentioned above, has already been noted. It is indirect, and can be treated by a repetition of the same operation, with or without a flap, or narrowing of the external ring, as may be thought desirable. A method described of reinforcing a weak external oblique by pleating I have discarded as being quite unsound, in that contraction of the external oblique pulls the fibres of the aponeurosis into parallel line and thus tears away the pleats and further weakens the fascia.

I believe that a direct hernia following an invagination operation is a new hernia and unrelated to the original operation.

Bassini Operation.

The Bassini operation is followed by two types of recurrence: (i) indirect (the commonest)—the explanation of this would appear to be failure to find the sac at the original operation; (ii) direct, in which the scar breaks down; this recurrence is usually situated laterally towards the internal ring, in front of the femoral vessels.

I believe that the Bassini operation is bad in theory, in that it is unphysiological to sew the internal oblique to the inguinal ligament, as contraction of the muscle pulls the two structures apart and must lead to atrophy of the sewn portion of muscle. It is furthermore still a matter of contention, to say the least of it, whether muscle will unite with tendon or fascia. When the transversalis fascia is inefficient in the outer part, and destruction of the lower part of the internal oblique has occurred, the external oblique aponeurosis, weakened by scar as the result of its division, is unable to withstand the intraabdominal pressure, and a direct hernia results. This operation is mutilating and in no way restores or reinforces the normal mechanics of the inguinal canal. In my opinion it should be discarded.

The operative repair of recurrent herniæ after the Bassini operation may present problems that will fully tax the skill and ingenuity of the surgeon. For example, in the direct type the field consists of a mass of scar tissue lying in front of the femoral vessels, which are in close proximity. The lower fibres of the internal oblique have been destroyed and the overlying external oblique fascia has been scarred and stretched. The transversalis fascia has disappeared in the scar. When the scar tissue has been cleared out and removed, an often alarming gap presents itself for closure. It is thus no wonder that surgeons are happier to refer the patient to their friends or to the truss-maker.

I have in recent months used a full-thickness skin graft, cut from the margin of the incision, to bridge this gap, sewing the graft to the internal oblique above, to Thompson's ligament below and to the conjoint tendon medially, with the graft on moderate tension. Over this I have found it sometimes possible to close the external oblique fascia. At other times a rectus-sheath flap has to be utilized to reconstruct an anterior wall. While I have had the opportunity of employing this skin graft for hernial repairs on only a few occasions and over a period of a few months only, the immediate results appear to be so encouraging that this manœuvre gives promise of being the answer to one of the surgical problems which previously appeared almost insoluble. If future developments prove this procedure to stand up to its expectations, the scope for the use of the buried graft will no doubt extend to the repair of those herniæ in which there are a wide internal ring and a deficient lateral portion of the transversalis fascia, or even to the replacement of a complete deficiency of this layer in the case of the large direct herniæ. No doubt this is a more logical procedure than the lowering of the external ring, although, as has previously been mentioned, the result of the operation for transposing the external opening has been consistently good.

These remarks apply only to the direct recurrence, which is virtually an incisional hernia. When the recurrence is indirect—that is, when the sac has not been found at the original operation—invagination of the sac is a sufficient procedure, with or without reinforcement of the external ring.

Halsted Operation.

It is difficult to understand how the Halsted operation—which is basically a variation of the Bassini operation, depending on an anterior transposition of the cord, which is brought out in front of the external oblique aponeurosis—came into being; it produces a persistent direct opening from the abdominal cavity through the abdominal wall, a procedure contrary to all surgical principles. The inevitable result must be a direct incisional hernia.

Recurrence after the Halsted type of operation is a direct incisional hernia, and at operation the hernial sac is found lying in the subcutaneous fat with its neck at the internal ring, the margins of which are composed of adherent transversus and internal oblique muscle together with the external oblique fascia and the inguinal ligament. The amount of scarring here frequently makes separation of these muscles and fascia almost impossible. The sac varies in size, from small sacs having a capacity of one

to two ounces to large sacs with a capacity possibly of two pints, and I have seen many feet of small bowel contained in these larger sacs. After the sac has been freed and its neck oversewn, the cord structures are found on the medial side; they are usually considerably hypertrophied. Here again, scarring between the external oblique fascia and the posterior wall of the canal frequently precludes the possibility of replacing these cord structures in their anatomical position, deep to the external oblique, as this fascia cannot be sufficiently separated to be again brought in front of the cord. It then becomes necessary to repair the outer part of the posterior wall in front of the hernial opening, and for this purpose, a full-thickness skin graft is used, which is sewn to the margins of the opening, sufficient space being allowed for the exit of the cord. In addition, a new anterior wall of the canal must be constructed, and for this a rectus-sheath flap is cut with a lateral extension into the external oblique fascia, of a sufficient distance to allow this flap to be turned down and sewn to the inguinal ligament, from a point close to its pubic attachment medially to a further point sufficiently lateral to cover the hernial opening. Lateral to this the flap is sewn to the external oblique fascia. This procedure reconstructs an inguinal canal on the same mechanical principle as the normal canal, and in my hands has led to satisfactory results. The operation is difficult and tedious, and takes considerable time to perform.

After-Treatment.

Treatment following operation is reduced to the simplest possible; "Cellophane" applied directly to the wound is the only dressing. This "Cellophane" is comfortable and allows the wound to be inspected with the minimum of disturbance. Patients are usually allowed to get up on the following day, and certainly within forty-eight hours. I find that this is possible, provided that all suturing is done without tension. This is particularly important, as I feel sure that any stitches on a tension are likely to cut out, and thereby the surgeon's purpose is defeated. Patients are allowed to return to work at the end of a month, when efficient healing should have taken place. Furthermore, activity prevents disuse atrophy and maintains a strong and efficient abdominal wall. As a rough estimate, it can be stated that a month's incapacity follows each week of recumbency. It is obvious, then, that a period of three or four weeks in bed followed by three or four months' incapacity involves a high economic loss to the patient, to industry and to the community, and the period should, if it is reasonably possible, be reduced to a minimum.

I do not suggest that any type of operation, with our present knowledge, will obviate the possibility of a recurrence; but I do suggest that a clearer appreciation of the anatomy and mechanics of this intricate and efficient outlet mechanism (the inguinal canal) and an operation planned to conform with its normal structure—to reinforce and to restore rather than to reconstruct on a new plan—will lead to better operative results and to a reduced morbidity rate.

Reports of Cases.

HIRSUTISM OF ADRENAL ORIGIN.[1]

By RICHARD FLYNN,
Sydney.

IN this communication I am reporting a series of seven patients who sought medical attention because of hirsutism. In all there was some departure from the normal in the cortex of the suprarenal gland or glands. The series includes a "luxuriant adenoma of the cortex of the suprarenal" (Case III), a malignant tumour of the suprarenal (Case V), a cyst of the cortex of the suprarenal which may be looked upon as a degenerating adenoma (Case VI) and four examples of hyperplasia of the cortex of the suprarenal. The series is also interesting because of the fact that in two cases (Cases II and IV) of hyperplasia of the suprarenal pregnancy ensued and the patients have been delivered of healthy, normal-appearing children since the removal of the suprarenal. Rynearson has written that "many women are supposed to have a basophilic adenoma of the pituitary gland simply because of obesity and hirsutism"; he might as truly have written that the suprarenal cortex and ovary are as frequently suspected and, more rarely, tumours of the thymus and pineal gland.

What the clinician is seeking is some method by which from the many patients with obesity and hirsutism those with suprarenal abnormality may be selected. Owing to the work of Broster and his co-workers some progress has been made along these lines. At first they made use of a capon test for the examination of the androgenic activity. This test depended on the ability of an androgenic substance to stimulate the growth of the secondary sexual characters in a bird from which the normal source of male hormone had been eliminated by removal of the sex glands. This method of investigation, though admirable for a research institution, is not suitable for routine investigation of suspected cases in a busy hospital, so it is fortunate that biochemists have supplied us with a more rapid means of selecting patients suitable for adrenalectomy. Professor V. M. Trikojus, now head of the Department of Biochemistry, University of Melbourne, while on the research staff of the Department of Medicine, University of Sydney, kindly supplied me with the method which he adopted in the assay of the 17-ketosteroids in the urine. It is as follows:

> The method used was essentially that described by Callow, Callow, Emmens and Stroud[1] (1939), the carbon tetrachloride being removed each time by suction through a fine tube rather than by separation in a funnel. It was found that the m-dinitrobenzene was improved by *centrifuging* the alkaline alcoholic solution of the compound immediately the pink colour reached a maximum (see Callow and Callow,[2] 1938), carefully removing the clear liquor, precipitating with water and then recrystallizing.
>
> The standard used was a specimen of androsterone kindly made available by the Department of Biological Standards, National Institute for Medical Research, Hampstead, London, and the colorimetric comparisons were made in a Hilger Absorptiometer using green and violet filters.

Professor Trikojus has asked me to acknowledge his indebtedness to Miss B. McVicar, B.Sc., who greatly assisted him in the estimations, and also to express his thanks to the Australian National Health and Medical Research Council for financial assistance in the purchase of the Hilger absorptiometer for the colorimetric estimation of the ketosteroids in the urine of suspected patients. Since his transfer to Melbourne I am indebted to Dr. E. Day, biochemist of the Royal Prince Alfred Hospital, and to Dr. A. Bolliger, of the New Medical School, for the carrying out of the estimations.

Case I.

N.M.T., a single girl, aged seventeen years, was admitted on March 11, 1942, to the Royal Prince Alfred Hospital under the care of Professor C. G. Lambie. She complained of increasing weight, having gained four and a half stone in the previous three years, and of excessive hair on her face and chest, which she had noticed during the preceding three years. Her menstrual periods had commenced when she was thirteen years old and had been regular for one year; then she had had amenorrhœa for one year, and since then the menstrual periods had been grossly irregular, occurring sometimes every five weeks, but more frequently at intervals of three months. Inspection of the patient showed that she was obese, that there was an excess of hair on her face and limbs, that the distribution of her pubic hair was of the male type, and that the proximal portions of toes and fingers were covered with hair. She weighed 10 stone 12 pounds.

Examination of the patient showed that her systolic blood pressure was 130 millimetres of mercury and her

[1] Accepted for publication, January 23, 1946.

diastolic pressure 100; her pulse rate was 80 per minute. Her breasts were well developed, and around the areola of the breasts there were a number of long hairs. The palms of her hands and the soles of her feet were moist. Otherwise no obvious departure from normal was observed on physical examination.

The following laboratory investigations were carried out. The blood sugar level before the ingestion of glucose was 88 milligrammes *per centum*; half an hour after the ingestion of 50 grammes of glucose dissolved in 100 millilitres of water it was 124 milligrammes *per centum*; after one hour it was 100 milligrammes *per centum*; after one and a half hours it was 70 milligrammes *per centum*; and after two hours it was 124 milligrammes *per centum*. The basal metabolic rate was −10%. The radiologist reported that the appearances in the skiagram of her pituitary fossa were normal, that an excretion urogram showed that both kidneys were secreting the dye regularly and that they were regular in outline, size, shape and position, and also that skiagrams of her knees showed that the epiphyseal lines were completely fused and that no abnormality was present around either knee joint or the right wrist. Estimation of the androgen content of her urine was carried out before operation by Professor Trikojus, and the results are as shown in Table I.

TABLE I.

Date of Taking of Specimen.	Volume of 24-Hour Specimen. (Millilitres.)	Date of Assay.	17-Ketosteroids. (Milligrammes per Litre.)	17-Ketosteroids. (Milligrammes in 24 Hours.)	Date of Operation.
2/4/42	1,930	6/ 8/42	18·0	34·7	12/12/42
17/11/42	2,050	8/12/42	8·8	18·0	

It was decided to explore the patient's abdomen, so accordingly she was given sodium chloride, 10 grains in gelatin capsules three times a day.

On November 26, 1942, I examined the patient's pelvis under general anæsthesia; her uterus was of normal size and no palpable masses were detected in either fornix. A cystoscopic examination was made at the same time; her bladder was normal and a differential function test of her kidneys with indigo-carmine showed that both kidneys were secreting the dye normally. Retrograde pyelograms were of normal appearance.

Exploration was decided on, so through a right-sided subcostal incision the abdomen was explored. The pelvic organs were normal as far as could be ascertained by palpation, and as no mass could be felt in the left suprarenal area it was decided to remove the right adrenal, in the belief that the case was one of hyperplasia. She stood the operation well; but progressive recordings of her blood pressure showed a distinct fall after the adrenal gland had been palpated and its blood supply interfered with. A blood transfusion was given; but it was several hours before her blood pressure reached its pre-operative normal.

Dr. F. B. Byrom reported on the excised gland. On macroscopic examination he found that the specimen consisted of portion of the adrenal gland and of some of the surrounding adipose tissue. The adrenal cortex measured 0·2 centimetre in depth and the medullary tissue appeared to be small in amount. On microscopic examination he found that the cortex, which was not increased in depth, was divided into two approximately equal parts, the outer of which, comprising the *zona glomerulosa* and *zona fasciculata*, was composed of apparently normal cells loaded with lipoid. The inner half—the *zona fasciculata*—consisted of cells which contained no visible lipoid, the cytoplasm being deeply eosinophilic. A few small cortical adenomatous nodules were present in the capsule. The medullary tissue appeared normal in amount. No fuchsinophile material was observed in sections stained by Vines's technique. Dr. Byrom remarked that the lack of suitable control tissue made it impossible to decide whether the appearances were normal or not.

Post-operative estimations of the ketosteroids in the patient's urine on December 13 and 17, 1942, and on January 5, 1943, gave figures varying between 8·5 and 9·3 milligrammes per litre.

The patient was recently examined and asked whether the operation was worth while. She replied that she was not so vague as previously, when she might be doing something with her mind 100 miles away; now she was more inclined to do things and on the whole the operation had been well worth while. She has lost no weight, but the hirsutism is growing less. Her menstrual periods occur regularly every twenty-eight days and last for three or four days.

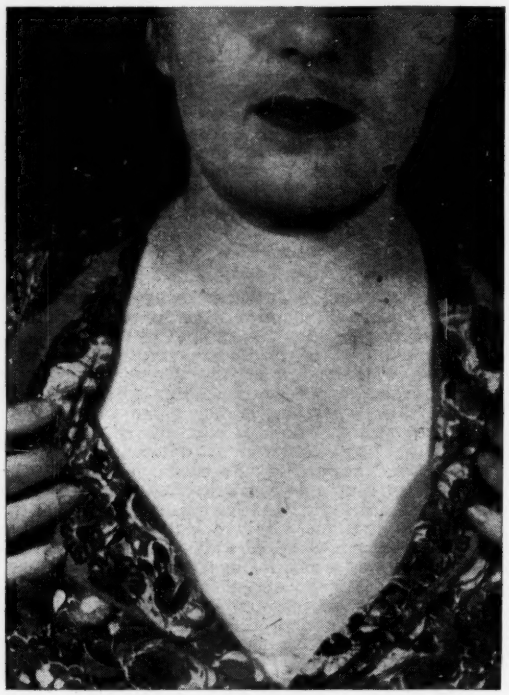

FIGURE I.

Case II.

N.H., a female patient, aged twenty-two years, was referred to me by Dr. Joseph Coen for investigation of the cause of her facial hairs, with a provisional diagnosis of adrenalism. She had consulted various doctors before Dr. Coen examined her and had been advised to take thyreoid tablets. Her menstrual periods were regular, but in some months the amount lost was much less than in others; the periods usually lasted four days and she usually had pain on the first day, but did not need to stay in bed. The last menstrual period had occurred three weeks previously. She had had many facial hairs removed by experts, but they always returned. She weighed ten stone one pound, and she was gaining in weight. She had first noticed hirsutism when she was aged fourteen years (her menstrual periods had commenced at fourteen years); at first the hair was just down, but later it was coarse and black (Figure I). At first the down was long, but the hair on the face and neck was now black, while the hair on her scalp was fair. She had hair on her chest and the distribution of pubic hair was male in type. The hair on her legs was thick and she also had some hair over the proximal phalanx of her fingers and toes (Figure II). Her blood pressure, estimated in the customary manner, was 110 millimetres of mercury (systolic) and 75 millimetres (diastolic). Pelvic examination under anæsthesia disclosed

no abnormality, and the clitoris was not hypertrophied. The basal metabolic rate was −20%. Excretion urography revealed complete duplication of both kidneys, all of which had complete ureters. Professor Trikojus estimated the ketosteroids in her urine on four occasions; on January 14, 1943, the content was 21·4 milligrammes per litre, and on three other occasions the figures were respectively 18·3, 17·2 and 6·2 milligrammes per litre.

On February 6, 1943, through a Kocher incision in the right subcostal region, the right suprarenal gland was removed. Some shock was experienced during the operation. Recovery was uneventful and the hair was easily removed on the third day. Estimation of ketosteroids on two occasions after operation gave the following figures: February 16, 3·5 milligrammes per litre; March 16, 11·1 milligrammes per litre. The patient married on February 6, 1945, and reported to me on May 22, 1945, when I found her to be pregnant. She placed herself in the care of Dr. Bruce Williams, and on January 10, 1946, she was delivered of a healthy male child.

FIGURE II.

Case III.

C.H., a female patient, aged thirteen years, consulted Dr. Harold Ritchie on account of hirsutism. The hairs had first appeared at the age of ten years, and since the age of twelve years the child was accustomed to get up and shave at 2 a.m. so that her family would not know of her difficulty. Investigation of her previous history disclosed the fact that a gynæcologist had admitted her to hospital and after examination under anæsthesia had dismissed her. She had never had a menstrual period.

On examination the patient had an extraordinary growth of hair, masculine in distribution, on the face, pubes and chest (Figures III and IV show this). The clitoris was greatly hypertrophied, the size of a small penis, and in the right loin could be felt a ptosed kidney with some suggestion of a mass above it. Her voice was harsh and masculine and her bodily build was masculine. Her systolic blood pressure was 130 millimetres of mercury and her diastolic pressure was 60 millimetres. An excretion pyelogram was prepared by Dr. B. P. Anderson Stuart, who reported as follows:

> The right kidney is very mobile and ptosed. The ptosis in the vertical position was very marked, the lower pole of the kidney lying well below the level of the iliac crest. There is no evidence of calculus or hydronephrosis and the kidneys appeared to be functioning satisfactorily. The upper pole of the right kidney is not sharply outlined in any of the films, and there appears to be a little indentation of the border of the psoas muscle. This might be possibly due to an enlargement of the suprarenal on this side.

The child's parents were greatly troubled about her because she had had no schooling and they were desirous of sending her to boarding school. A tentative diagnosis of suprarenal tumour was made by Dr. Harold Ritchie, and I was invited to take over the patient at this point. She was admitted to Gloucester House on February 15, 1943. X-ray films of her left knee and elbow joints on February 23 revealed that all the epiphyses in both joints had joined the diaphyses. Professor Trikojus estimated the 17-ketosteroids in twenty-four hour specimens of her urine on several occasions, with the following results (Table II):

The provisional diagnosis of adrenal tumour was strongly supported by these findings and the child was prepared for operation. The administration of capsules containing sodium chloride (10 grains) and sodium citrate (10 grains) was commenced on March 19. On March 30, under nitrous oxide and oxygen anæsthesia, a right subcostal incision (Kocher) was made and a large tumour

FIGURE III.

was found. It was situated immediately below the liver and was retroperitoneal in position, displacing the duodenum medially, and the kidney was posterior to the tumour. The uterus was small, as were both ovaries. The left suprarenal appeared to be normal on palpation. The tumour was removed without difficulty; it weighed 480 grammes, almost one pound (Figure V). She was given a blood transfusion and 1,000 millilitres of normal saline solution with 10% glucose solution during the operation. Her pulse rate at the end of the operation was 120 per minute. Dr. Hercus took half-hourly records of her blood pressure for the first twenty-four hours; it was usually 90 millimetres of mercury (systolic) and 60 millimetres (diastolic), and it was twenty-four hours before the pre-operative pressure was reached and maintained. During the first twenty-four hours after operation her pulse rate varied between 100 and 128 per minute. Except for a slight rise in temperature during the first week her convalescence was uninterrupted and she was discharged from hospital on May 6. She was kept in hospital for so long because she lived in the country, and in order that an estimation of the ketosteroids in her urine could be made in the immediate post-operative period.

On April 2, the third day after operation, the patient asked: "Do you think these hairs are softer? Because I do." The hairs on her face were easily pulled out on that day.

Dr. F. B. Byrom made a pathological examination of the tumour. To the naked eye it was an unfixed, ovoid tumour bounded by a thin, grey, fibrous capsule; it weighed 481 grammes. On section the tumour was found to consist of soft, opaque, plum-coloured tissue resembling that of a spleen, in which were areas up to 0·5 centimetre

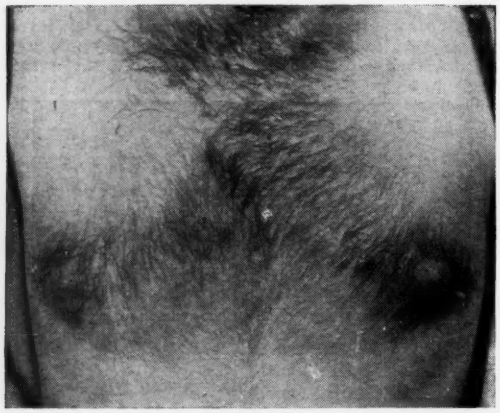

FIGURE IV.

in diameter of dark red hæmorrhage. There were also a few areas up to 0·4 centimetre in diameter of opaque yellow tissue, and one zone of gelatinous grey tissue resembling white of egg (Figure V). Histologically the tumour was found to be a luxuriant adenoma of the cortex of the suprarenal gland. It was composed of large polyhedral cells, mostly in the form of a continuous mosaic, but showing a tendency to form radial strands in the

TABLE II.

Date of Taking of Specimen.	Volume of 24-Hour Specimen. (Millilitres.)	Date of Assay.	17 Keto-steroids. (Milli-grammes per Litre.)	17-Keto-steroids. (Milli-grammes in 24 Hours.)	Date of Operation.
16/2/43	2,040	12/3/43	530	1,080	
17/2/43	1,620	12/3/43	660	1,070	30/3/43
19/2/43	930	12/3/43	900	837	
Average of 10 days	937	30/4/43	1,020	956 (10 days before operation)	

TABLE III.

Date of Taking of Specimen.	Volume of 24-Hour Specimen. (Millilitres.)	Date of Assay.	17-Keto-steroids. (Milligrammes per Litre.)	17-Keto-steroids. (Milligrammes per 24 Hours.)
16/4/43	2,160	30/4/43	3·5	7·7
17/4/43	1,970	30/4/43	4·8	9·45

periphery of the tumour. In many areas the mosaic was infiltrated with recent hæmorrhage, possibly due to operation, and towards the centre of the tumour there were large areas of extremely œdematous collagenous tissue containing discrete tumour cells. The capsule consisted of dense collagen containing abundant venous tissue and occasionally partly occluded arteries. The capsule had not been invaded by growth. The tumour cells had abundant cytoplasm consisting of confluent, medium-sized, eosinophilic granules. The nucleus in most cells was centrally situated, small and round, with a fairly clear chromatin network and from one to three distinct nucleoli (Figure VI).

However, there were considerable numbers of large, pyknotic and double nuclei throughout the tumour. In sections stained by Vines's technique the cytoplasm had a grey, granular appearance.

Dr. Byrom commented that the tumour closely resembled those found in the inner zones of the suprarenal cortex. There was no direct histological evidence of malignant change, but many of the tumour cells were atypical.

On August 24, 1943, I noted that the patient still had much hair on her face, but it was softer and finer than before; her breasts had increased in size and she had had

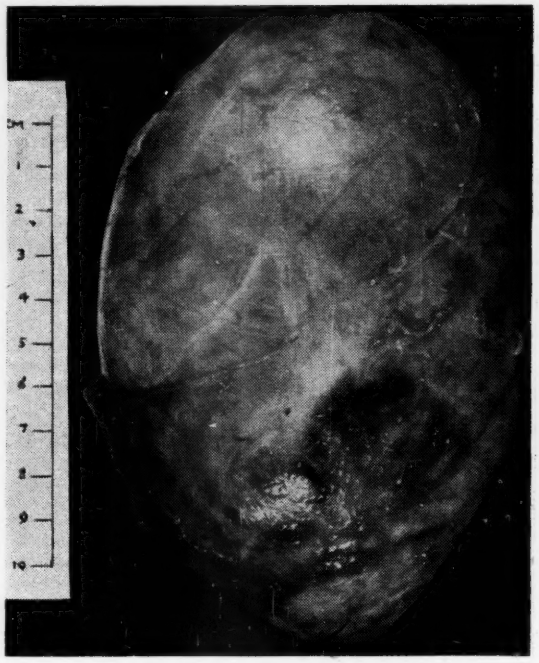

FIGURE V.

three menstrual periods since operation, the first about the end of June, the last two weeks previously. Her voice was much softer and there had been an enormous loss of hair from her body (Figures VII and VIII). On December 17, 1943, the blood pressure was 100 millimetres of mercury (systolic) and 60 millimetres (diastolic). Her breasts had still further enlarged. The menstrual periods had been regular at intervals of twenty-eight days; they lasted for four or five days and she used three or four diapers per day. She had no headaches and with a characteristic note of triumph she said that her menstrual periods were "just as good as gold"—a sympathetic reference to her less fortunate school mates. During 1944 she maintained her symptomatic improvement, and it is interesting to note that she passed with honours a music examination (Grade III, vocal section for female voices). The ketosteroids in her urine were estimated again by Dr. Day, who reported the figure of six milligrammes per litre; it therefore appears at present that the tumour was benign. A further note on the hirsutism on her face and neck states that it was much less obvious, though still present. I am assured that American dermatologists report that shaving does not increase the coarseness of the hair, so that when the patient reaches the "age of vanity" it will be interesting to see what method she adopts to placate the natural urge.

Case IV.

K.M.S., a married woman, aged twenty-six years, was referred to me by Dr. Frances McKay, who suspected that she had a suprarenal lesion on account of the excessive hair on her face and body. When the patient was a girl of fourteen to sixteen years she had a slight amount of hair over the upper lip; then, at about the age of eighteen years hair began to grow on her chin and on her chest (Figure IX). This hair had become more and more profuse and coarse ever since then, and was also appearing in new places and extending further. The patient married at the age of twenty-one years, and shortly afterwards she began to suffer from menorrhagia; the menstrual periods also occurred very close together (about every ten to fourteen days), which meant that she was almost continuously menstruating. She was operated on in her home town for cystic ovaries, the cysts being removed, and her appendix was also removed. Since then her menstrual periods had been very irregular and at times there were intervals of some months between them. They lasted for six to eight days. The patient had had bladder trouble for six to seven years, experiencing burning and scalding on micturition, and frequency, and occasionally hæmaturia.

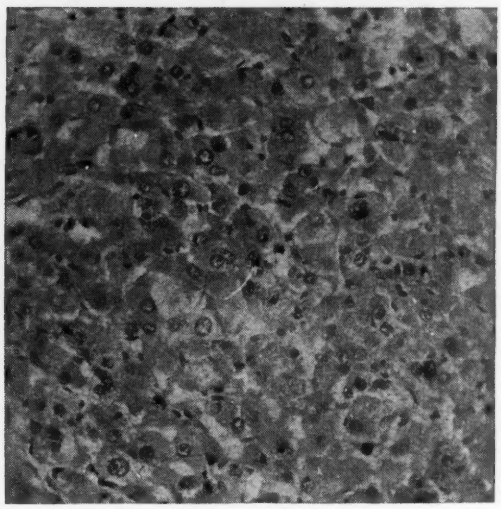

FIGURE VI.

The following laboratory investigations were carried out. On March 2, 1943, the blood urea level was 54 milligrammes *per centum* and the blood cholesterol content was 112 milligrammes *per centum*. On March 19 the fasting blood sugar content was 97 milligrammes *per centum*; half an hour after the ingestion of 50 grammes of glucose dissolved in 100 millilitres of water the blood sugar content was 126 milligrammes *per centum*; after one hour it was 124 milligrammes *per centum*; after one and a half hours it was 120 milligrammes *per centum*; and after two hours it was 120 milligrammes *per centum*. The basal metabolic rate was −15%. The radiological report on a skiagram of the patient's skull stated that the pituitary fossa was rather large, but within normal limits. No abnormality was detected in a skiagram of her chest. An excretion urogram showed that her kidneys were normal in size and shape and secreted normally, and these findings were confirmed by retrograde pyelograms. A Graham's test showed that the gall-bladder was normal in size, shape and position, that it functioned normally and that it contained no calculi. Ketosteroid estimations were carried out by Professor Trikojus, with the following results (Table IV):

On account of the clinical features and the result of the laboratory investigations, I advised her to allow me to explore her abdomen. She accepted the advice, and on April 1, through a right subcostal incision, I carried out the exploration. The uterus and ovaries by palpation appeared to be of normal size, and no obvious tumours were palpable in her suprarenal glands. So, in the belief that simple hyperplasia was present, I removed her right suprarenal gland with difficulty. Her convalescence was easy and uninterrupted.

Pathological examination of the excised tissue gave the following findings. Macroscopically the specimen was seen to consist of numerous pieces of yellowish tissue measuring approximately 3·0 by 1·5 by 0·25 centimetres. On cross-section the cortex did not seem to be enlarged and the medulla was inconspicuous. Examination of sections prepared from the specimen revealed yellow pieces of tissue (suprarenal), some of the pieces having adipose tissue attached. The weight was five grammes. On microscopic examination the histological appearances were similar to those seen in the previous cases. The cortex, which was not thickened, was composed of two layers of approximately equal thickness. Of these, the outer was composed of polyhedral foam cells, while the inner consisted of cells of which the cytoplasm was granular, eosinophilic and free from lipoid. The cytoplasm in the latter cells stained greyish-orange by the Vines-Ponceau fuchsin method. The medullary tissue appeared normal.

FIGURE VII.

After operation the patient showed great improvement. Her face became softer and more feminine looking, she lost great rolls of fat from around her back and shoulders, the hair on her body was much less, and though hair was still noticeable on her face, it was much less coarse and of a lighter colour. The patient herself was well satisfied with the improvement (Figure X). She returned to hospital on July 25, 1944, because she hoped that she was pregnant and was fearful lest the abdominal pain which she was experiencing might be due to a threatened miscarriage. I took the opportunity of having the urinary ketosteroid excretion estimated. Dr. Day reported the finding of 11·9 milligrammes in a twenty-four hour specimen. As the patient's menstrual periods had been present a month previously, and for the interest of the matter, I asked for an Aschheim-Zondek test of her urine. Dr. Day, employing the Freidman's modification of the test, reported a positive result. The patient was congratulated and was advised to rest for a month in bed at home; this she was willing to do. She placed herself in the care of Dr. Frances McKay, who informed me that on March 16, 1945, our patient was delivered of a daughter.

TABLE IV.

Date of Taking of Specimen.	Volume of 24-Hour Specimen. (Millilitres.)	Date of Assay.	17-Keto-steroids. (Milli-grammes per Litre.)	17-Keto-steroids. (Milli-grammes in 24 Hours.)	Date of Operation.
5/3/43	2,360	20/3/43	5·0	11·8	1/4/43
22/3/43	2,700	7/4/43	6·7	18·1	
25/3/43	2,710	7/4/43	6·0	16·3	

Case V.

N.M.A., an unmarried female patient, aged thirty-one years, was admitted to the Royal Prince Alfred Hospital on August 4, 1943, under Professor C. G. Lambie, with a provisional diagnosis of pituitary dystrophy. She stated that during the last four years she had been increasing in weight and that her menstrual periods were decreasing in the amount of the loss and in duration, but remained regular, occurring every thirty days. She was also disturbed by the presence of a profuse growth of long black hair on her cheek, chin and upper lip. She complained of pain in the left inguinal region, which was worse on exertion and was occasionally aggravated by a backache. It was worse at menstruation, beginning to increase in intensity from the onset and becoming unbearable in the early stages. Her menstrual periods had commenced when she was sixteen years of age, and at that time they occurred regularly every thirty days and she had no dysmenorrhœa. Pain and scalding on micturition during menstruation had been noticed, but no frequency. She had no other complaints.

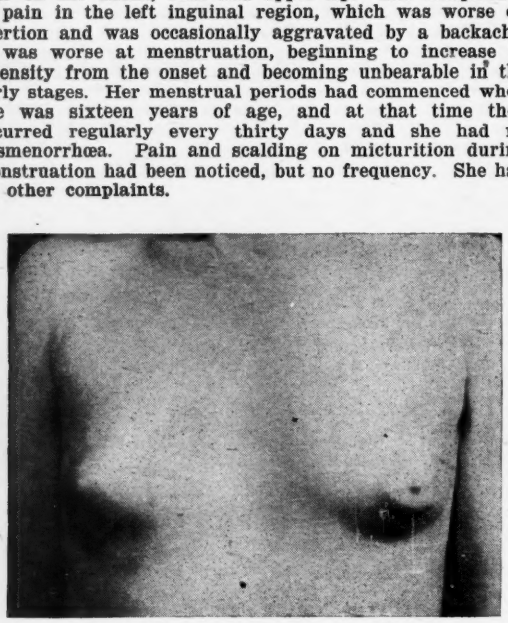

FIGURE VIII.

On physical examination of the patient her blood pressure was 140 millimetres of mercury (systolic) and 80 millimetres (diastolic), recorded in the usual manner. No masses were palpable in her abdomen. Laboratory examinations included a blood count, which revealed that the red blood cells numbered 5,250,000 per cubic millimetre, the hæmoglobin value was 96% and the white blood cells numbered 14,100 per cubic millimetre; a neutrophile leucocytosis with a slight shift to the left was present. The blood sugar estimation and sugar tolerance tests gave normal results. The basal metabolic rate was −14%. The blood urea estimation and urea concentration tests also gave normal figures. A skiagram of the *sella turcica* revealed no enlargement, and an excretion urogram revealed no abnormality in the plain X-ray film and faint filling only of the kidneys; the calyces and pelvis appeared normal; the kidneys were normal in size and shape, and both ureters appeared regular; no shadow of a calculus was seen. A skiagram of the lumbar portion of the spine and the pelvis revealed no abnormality. A barium enema was given and X-ray examination revealed that the enema flowed freely to the caecum. The sigmoid colon was slightly spastic but there was no definite evidence of diverticula in that area. Estimation by Dr. Day of the amount of 17-ketosteroids in a forty-eight hour specimen of urine, collected by an indwelling de Pezzer catheter, showed that the amount was increased; it was 28 milligrammes per litre, as compared with the normal figure of 8·0. Pelvic examination with the patient under anæsthesia revealed that the uterus was small and in normal position and that no abnormal masses were palpable in either fornix. On account of the clinical picture and the increased excretion of ketosteroids, Professor Lambie transferred her to my care for abdominal exploration, suspecting an adrenal lesion. The pre-operative treatment included a diet poor in potassium and a blood transfusion, and she was given three times a day gelatin capsules containing sodium chloride (20 grains) and sodium citrate (five grains) three times a day. On the morning of the operation she was given intravenously 1,000 millilitres of 5% glucose and saline solution, and intramuscular injections of three millilitres of "Eschatin" and one millilitre of "Percorten".

On November 19 I explored her abdomen through a right subcostal incision. The right ovary contained a cyst which was palpated and seen; otherwise the ovary was normal. The left ovary was not seen, but it felt normal. The adrenals felt as if they were enlarged, and the left

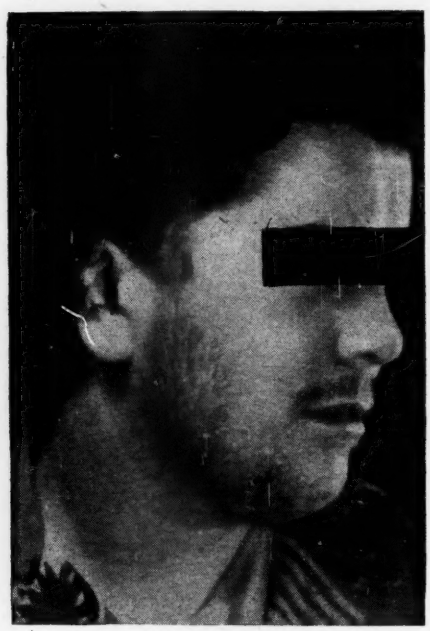

FIGURE IX.

appeared to be larger than the right. A provisional diagnosis of suprarenal hyperplasia was made at this time. Her gall-bladder contained three large stones and was an obstacle to exposure of the right adrenal, so it was removed without difficulty. Because of the high-lying kidney and the low-lying, enlarged liver, exposure of the right adrenal was unsatisfactory, so it was decided to stop the operation and to remove the left suprarenal through a posterior approach at a later date. The patient's condition at the end of the operation was only fair, probably because of the degree of pressure to which the adrenal had been subjected, so desoxycorticosterone acetate ("D.O.C.A.") was given and the dose was repeated as necessary. The patient was discharged from hospital, well, on December 16.

She was readmitted to hospital on January 11, 1944, After the same preparation as for the previous operation, the left suprarenal was exposed through a left lumbar incision. About four inches of the last rib were removed subperiosteally and then a satisfactory exposure of the suprarenal was obtained. As it was exposed it was seen that it contained a small, discrete tumour about the size of a large pea. The adrenal was removed easily; but the patients' systolic blood pressure fell to 80 millimetres of mercury, so she was given an intramuscular injection of "Percorten" and a blood transfusion, which was followed by a litre of normal saline solution. Next day her

blood pressure was 135 millimetres of mercury (systolic) and 90 millimetres (diastolic). On the second post-operative day her temperature rose suddenly to 105° F. Examination of her chest revealed a pyopneumothorax, the presence of which was confirmed by X-ray examination. Aspiration was performed and she was given "M & B 693" in suitable doses, but her condition gradually became worse and she died on the eighth day after operation.

Autopsy.

A post-mortem examination was carried out. The thyreoid gland was found to be rather large, but it was normal in consistency and colour. The thymus was not seen in the anterior mediastinal fat. The right kidney, which weighed 380 grammes, was much larger than usual and somewhat swollen, the renal substance protruding when the capsule was incised. In the cut surface some congestive changes were apparent. The pelvis and ureter appeared normal. The left kidney, which weighed 300 grammes, was also somewhat enlarged, but not to such a pronounced degree as the right. At the upper pole there

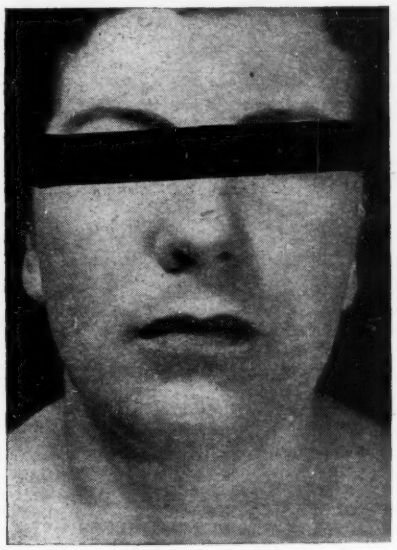

FIGURE X.

was a small tear in the capsule, which had been made at operation. In the cut surface were found essentially the same changes as in the right kidney. The right adrenal was slightly enlarged. When it was incised, a firm, fleshy tumour was disclosed, measuring about four by three by three centimetres (Figure XI). Its cut surface was pale and homogeneous and appeared cellular. The left adrenal had been removed at operation. The bed of the organ contained a small quantity of coagulated blood and a small, narrow sinus passed from it to the surgical incision in the left flank.

Histological examination gave the following information. An organizing hæmatoma replaced the greater part of the right adrenal; it was surrounded by a fibrotic capsule, in which was a little normal adrenal cortical tissue. No tumour was present. The pituitary was large, but showed no special histological changes. The ovary contained some *corpora albicantia* and a small follicular cyst, but no *corpora lutea*.

Dr. J. S. Robertson made a pathological examination of the tissues, with the following findings. In the thyreoid the acini were mostly large with low epithelium and well filled with colloid. No increase of fibrous tissue was noted. In the pancreas islets of Langerhans were numerous, large and easily found; they showed no special changes. Slight fatty infiltration of the secreting lobules was observed. The left adrenal gland was an operation specimen. On macroscopic examination it was seen to consist of an irregular mass of adipose tissue enclosing the adrenal gland, the latter measuring approximately 3·0 by 2·0 by 1·5 centimetres.

In the gland yellow lipoid-containing cortical tissue was visible around the periphery as a folded layer varying in thickness from 0·1 cm. to 0·3 cm. Internal to this layer, and occupying the centre of the gland, was homogeneous, soft, rather crumbling grey tissue, with here and there a small darker hæmorrhagic area. No medullary tissue could be distinguished. Microscopic examination: In the lipoid-containing outer zone the normal anatomical arrangement had been lost. Although there was a slight attempt at the formation of cellular columns, there was no tendency towards the alignment of the columns perpendicular to the surface, the cellular arrangement being almost a continuous sheet. The cells themselves were polyhedral or spindle-shaped, and there was little intercellular stroma apart from the numerous thin-walled capillary channels traversing the tissue. The nuclei varied in size, being in general round or ovoid, but sometimes elongated, with a usually clear chromatin network. The cell cytoplasm was clear and contained lipoid. Occasional cells were much larger, with several nuclei. Some small areas of recent hæmorrhage were also visible.

This outer zone passed with considerable abruptness into the inner zone, which occupied the centre of the gland, and which appeared grey to the naked eye. Here the tissue had undergone coagulation necrosis, the cell outlines being still visible. Around the periphery of this necrotic central mass were numerous large cells containing brown pigment granules. Occasional similar pigment-laden cells were present in the inner necrotic zone. Mitotic figures were visible in the outer zone, and this fact, together with the nuclear and cellular pleomorphism, suggested that the gland was the seat of a carcinoma. It appeared to conform most closely to the type described by Vines as "carcinoma simplex", in which there is no attempt at organoid arrangement, and in which giant cells and extensive necrotic areas are commonly seen. In sections stained by Vines' method, red staining was confined to red blood cells in the hæmorrhagic areas.

Case VI.

J.McG., an unmarried woman, aged thirty-two years, sought medical care on account of obesity and hirsutism. She stated that she had been excessively fat for as long as she could remember; at the age of twelve years she weighed about 11 stone and at twenty-three years she weighed 24 stone. She had noticed excessive hair corresponding to the male distribution since she was about twelve years old. Her menstrual periods had commenced when she was ten years old; they lasted three to four days and occurred at intervals of three to four weeks. She considered the quantity of discharge lost moderate. She also complained of frequent frontal headaches, of giddiness, of breathlessness and of sleeplessness. Her mother had become very fat after her marriage, weighing 20 stone. The patient had no sister, but she had six healthy brothers and one other who was born with muscular dystrophy. She had suffered from pneumonia as a child.

Physical examination confirmed the patient's description of her obesity, which was generalized, with a large apron of abdominal subumbilical fat. She had considerable excess of facial hair of a coarse reddish type. She had no hair on her forehead, and there was no excess of hair on her extremities; the body hair had a slight male distribution, but this was not pronounced. No abnormality was detected on examination of her central nervous system and of her cardio-vascular and respiratory systems. Her systolic blood pressure was 210 millimetres of mercury and her diastolic pressure 110 millimetres, estimated in the usual way. Her weight was 23 stone 8 pounds. Professor C. G. Lambie, in whose care she was, gave her a weight-reduction diet and thyreoid gland substance. She was also given some X-ray therapy to the pituitary and thymus areas. By September 11, 1944, her weight had been reduced to 18 stone 6 pounds. A number of laboratory investigations were undertaken. The blood sugar content

was estimated at 88 milligrammes *per centum*. The blood sugar level before the ingestion of glucose was 88 milligrammes *per centum*; half an hour after the ingestion of glucose it was 141 milligrammes *per centum*; after one hour it was 106 milligrammes *per centum*; after one and a half hours it was 115 milligrammes *per centum*; after two hours it was 104 milligrammes *per centum*. The basal metabolic rate was −22%. The blood cholesterol content was 146 milligrammes *per centum*. A urea concentration test gave results within normal limits. The blood coagulation time was normal. A skiagram of the pituitary fossa revealed no abnormality. An excretion urogram on April 26, 1944, showed that the kidney shadows were normal in size, position and shape; the kidneys functioned normally and the anatomy was normal. There was no evidence of any abnormality, and nothing to suggest any tumour in the region of the adrenals. A skiagram of the chest revealed no evidence of any mediastinal growth or other lesion. Several estimations of the urinary excretion of 17-ketosteroids were made; on May 4, 1944, the figure was 11·6 milligrammes in twenty-four hours; on June 23 it was 6·5 milligrammes in twenty-four hours; on September 19 it was 15 milligrammes in twenty-four hours; on October 18 it was 13·5 milligrammes in twenty-four hours; on December 7 it was 9·6 milligrammes in twenty-four hours. Professor Lambie made a diagnosis of suprarenal lesion and transferred the patient to my care for surgical exploration.

FIGURE XI.

On September 28, through a subumbilical median incision, the abdomen was explored. Both ovaries were small and fibrotic; the uterus was normal. On palpating the adrenals I thought that the left was larger than the right. The appendix was removed and the abdomen was closed. On October 26, after the patient had been up and about for a week, operation was undertaken through a left lumbar incision to remove the left suprarenal. An unexpected finding was a large cyst of the suprarenal (Figure XII). The suprarenal was removed without difficulty.

The patient left hospital on December 6; her menstrual period was just over, and her weight was 17 stone. The next menstrual period occurred three weeks later, and since then the periods have occurred at regular intervals. The discharge is copious; the periods last five days and the patient sometimes loses clots. Some abdominal pain is experienced on the first day, but this is not so severe as before operation. The actual flow is heavier than before operation. Although she tries to adhere to her diet, the patient has broken it often, and consequently has gained ten pounds in weight in the past four months. She says that the facial hair grows as fast as it ever did, but it is softer and finer and lifts out more easily. A little hair has appeared on the abdomen since the last operation, where previously there was none. The hair on her chest has disappeared almost entirely; it was never thick. In general, the patient says that she feels better, works better and does not tire as easily as she used to. Her family notices a great improvement in her.

Dr. J. S. Robertson made a pathological examination of the specimen. He found it to consist of an adrenal gland, measuring with attached adipose tissue 10·0 by 4·5 by 2·5 centimetres. On section the gland was seen to be cystic; it was made up of a thin zone of yellow cortical tissue, about 0·2 centimetre in thickness, immediately bounding a central unilocular cystic cavity. A small amount of pale medullary tissue was visible in one place, where the central cyst had not completely separated the opposing cortical layers. Microscopic examination revealed a rather dense fibrous capsule surrounding the gland. The three cortical zones were present. The cells of the *zona glomerulosa* and of the outer part of the *zona fasciculata* contained lipoid. The cells of the inner part of the *zona fasciculata* and of the *zona reticularis* had eosinophilic cytoplasm, which in some areas stained red by a slight modification of Vines's method. The *zona reticularis* abutted directly against the

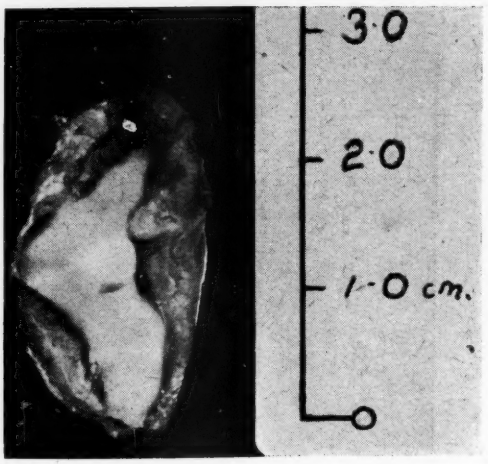

FIGURE XII.

central somewhat collapsed cystic cavity, although in some places small flakes of fibrin were present clinging to the cyst wall. In the small amount of medullary tissue present no special changes were detected.

Case VII.

P.S., a female patient, aged twenty-two years, was on April 19, 1945, referred to me by Dr. Harold Ritchie on account of hirsutism with a provisional diagnosis of suprarenal lesion. Her menstrual periods had begun when she was aged twelve years, and while she was at school they used to last five or six days and she was accustomed to use three or four diapers per day. At that time the periods were associated with little discomfort and no pain. She commenced her training as a nurse in 1939, and after about six months, when she was aged eighteen years, she noticed a change in her menstrual periods. She now had much pain with them, particularly on the day before and the first day. In 1942 she had amenorrhœa extending over a period of ten months, and after that her periods were very irregular in onset and occurred at intervals of about two months; they usually lasted for five days. She had first noticed hair on her face at the age of about twelve years, and it had gradually become coarser and of wider distribution. The hair was thick and dark, and she had to visit an expert hair remover at least once a week to keep herself feminine in appearance. She had recently noticed that the hair was becoming much thicker on her chest, arms and legs.

She was admitted to the Royal Prince Alfred Hospital under my care, and a number of investigations were carried out. A skiagram of the skull revealed no abnormality

in her cranial bones; the *sella turcica* appeared normal in size and regular in outline. A skiagram of her urinary tract showed no evidence of calculi, and urograms after the intravenous injection of iodide compound showed that both kidneys were secreting the dye satisfactorily and appeared regular. A skiagram of her chest was also of normal appearance. The basal metabolic rate was −12%. Her weight was 12 stone 2¼ pounds. Her blood sugar content was 115 milligrammes *per centum* and her sugar tolerance curve was of the "delayed" type. An estimation of her 17-ketosteroid excretion gave the figure of 20 milligrammes in a twenty-four hour specimen of urine.

On May 24, 1945, through a mid-line subumbilical incision, her abdomen was exposed. The uterus was of normal size and in good position, and both ovaries appeared normal. The left adrenal felt larger than the right, but there was little difference. I decided to remove her left suprarenal, and on June 28, through a left lumbar incision, the left adrenal was removed without difficulty. Dr. Day examined the excised suprarenal with the following findings. The specimen consisted of an adrenal gland measuring 7·0 by 3·5 by 0·5 centimetre; at one end it was folded back on itself; it appeared larger than normal and weighed 12 grammes. Examination of microscopic sections revealed a well-developed suprarenal; the various layers of the cortex and the cells of the medulla were well differentiated. Differential staining by Vines's method revealed medinsophile in the cells of the fasciculate layer of the cortex.

Convalescence was uninterrupted, and the patient was discharged from hospital on July 25. A post-operative estimation of her ketosteroid excretion on July 23, 1945, gave the result of 5·8 milligrammes in the twenty-four hour specimen.

The patient reported back at my request in January, 1946. She looked much improved, and the hirsutism was much less. She expressed herself as well pleased with the result. She informed me that she was beginning her midwifery training the next day.

Acknowledgements.

My thanks are due to my colleagues who referred their patients to me for operation, and to Professor V. M. Trikojus. The value of the report is greatly increased by the illustrations which accompany it, and for them I am grateful to Mr. Woodward-Smith, of the Medical Artistry Department, New Medical School, University of Sydney.

CURARE IN CONVULSIVE THERAPY.

By S. V. MARSHALL and CEDRIC SWANTON,
Sydney.

IN recent years curare has been used abroad to a considerable extent in therapeutics, notably for the prevention of traumatic complications in the convulsive therapy of various mental disorders. Before this time the application of the drug had been hampered by the lack of a standardized preparation, but now a reliable product, "Intocostrin" (Squibb), is available. This preparation contains 20 milligrammes of curarine per millilitre in watery solution, and it satisfies the necessary requirements of constancy of action and of freedom from undesirable side-effects.

Nevertheless, a thorough appreciation of the action of the drug is essential before its use is attempted, and due precautions must be taken against the possibility of respiratory paralysis, which is the chief danger. When suitable dosages are employed, this effect is virtually the only hazard involved, although overdosage is said to carry the additional risk of peripheral vascular failure. Therefore some means for the ready performance of artificial respiration with oxygen should accompany the use of curare, the best being a standard gas machine, with which adequate respiratory exchanges may be effected by the intermittent manual compression of the rebreathing bag.

Curare is one of the few drugs for which a true antidote is available. This is "Prostigmin", of which a dose of 0·25 milligramme given intravenously will produce an almost instantaneous and favourable response. With a careful technique in the administration of curare, however, the use of "Prostigmin" is rarely necessary. Adrenaline is also said to be of value, especially if any bronchospastic manifestation should develop — a reaction generally the result of overdosage with impure preparations. Ordinarily the timely intermittent inflation of the lungs with oxygen will tide the patient over the relatively transient period of depressed respiration or apnœa which may accompany the use of curare.

Clinical Record.

Mrs. I.S., a female patient, aged fifty-six years, had been suffering from involutional melancholia for more than eighteen months. At the onset of her illness she had fallen out of bed and fractured the neck of her left femur. This was corrected by the insertion of a Smith-Petersen nail, but after eighteen months there was little evidence of bony union. Physically she was otherwise healthy.

Because of the distressing degree of her mental symptoms it was decided to employ electro-convulsive therapy, but grave concern was felt about the likelihood of dislodging the nail in the course of this treatment. A decision was therefore made to use curare with the object of reducing the violence of the muscular spasms which are so prominent a feature of convulsive therapy. Various authorities were consulted beforehand, and a suitable procedure was formulated accordingly. The patient's general fitness for the presumed ordeal was appropriately assessed and all facilities for dealing with any emergency were provided.

In all, 11 treatments were given, with intervals of three or four days between each, as from December 1, 1945. No premedication was used. The routine posture was employed, with pillows beneath the knees and loins, and just before the shock was given a rubber mouth prop was inserted. The electrode was of standard type and was affixed during the process of posturing. On each occasion the electrical dosage was 140 volts for three-tenths of a second. No doubt the patient would have had a cortical discharge with a lesser voltage, but it was felt that a subconvulsive dose might necessitate further administration of curare and a repetition of the shock treatment.

Naturally the first treatment was embarked upon with great caution. First, the blood pressure was taken and the heart examined. The facilities for resuscitation were carefully checked over. Then a slow intravenous injection of "Intocostrin" was administered, a dose of 60 milligrammes being given over a period of five minutes; this was followed by a further 40 milligrammes given during the latter part of the next ten minutes. The effects, consisting of progressive generalized muscular relaxation together with pronounced ptosis and shallow diaphragmatic respiration, were anxiously noted. The convulsive seizure was then induced, a dosage of 140 volts for 0·3 second being employed. A remarkable reduction in the violence of the anticipated convulsive seizure, which lasted forty-five seconds, was apparent. No cyanosis occurred. Recovery followed the usual course, and contrary to expectations, there was no persistence of respiratory embarrassment. Although the radial pulse became imperceptible for about fifteen seconds at the height of the convulsive seizure, its volume and rate soon became normal, while a blood pressure reading taken ten minutes later gave normal figures.

The subsequent treatments were equally satisfactory in their results, although slight variations in the muscular response were noticeable. At no time was this of sufficient violence to cause anxiety about the stability of the nail in the femur. Usually there was moderate generalized stiffening, followed by only slight clonic twitchings, and even at the height of the tonic stage all limbs could be moved easily about their joints without force. The jaw could be readily opened and shut with light pressure. Asphyxial rigidity was never observed. An attempt was made to ascertain the optimum rate for injection of the

curare. This was found to be about two millilitres (40 milligrammes) per minute. When the curare was given rapidly the patient complained of unpleasant subjective sensations—a feeling of helplessness and impending suffocation—whereas if it was given slowly a larger quantity was required to produce the desired effect. Apparently in the latter case excretion was overtaking its delivery into the blood stream. Thus the dosage varied somewhat with the speed of administration; the range was from 80 milligrammes to 100 milligrammes and the periodicity from three to fifteen minutes, the optimum figures in each case being 85 milligrammes and five minutes respectively. This is somewhat in excess of the recommended dosage of five milligrammes per ten pounds of body weight, which in this case would have worked out at 70 milligrammes. Consequently it was found best to employ an approximation in dosages and to rely on the clinical response of the patient as a guide. As a rule pronounced ptosis and a virtual inability to lift the head were regarded as the signals for interrupting the injection and for giving the shock. A most remarkable feature was the speedy restoration of strong breathing once the immediate effects of the shock had passed off. It seems that the shock itself has an antidotal effect to the curare—that the intense nervous stimulus causes such an outpouring of acetylcholine at the neuro-muscular junctions as to neutralize effectually most if not all of the curare located there.

As the treatment proceeded the patient's mental condition steadily improved. The virtual abolition of the convulsive element did not appear to reduce the efficacy of the therapy. In the last few treatments she was somewhat apprehensive beforehand, especially in anticipation of the interim between the commencement of the injection and the induction of convulsions. This feature was likened by the attending sister to the "aura" characteristic of "Metrazol" shock. No alarming incident occurred at any stage of the treatment.

Conclusion.

The patient eventually made an excellent recovery from her mental disorder, and she is now enjoying a normal kind of existence. Her fracture suffered no disturbance, so that in view of these considerations we feel justified in claiming that the whole procedure was eminently satisfactory and successful.

Bibliography.

A. E. Bennett: "Preventing Traumatic Complications in Convulsive Shock by Curare", *The Journal of the American Medical Association*, Volume CIV, January 27, 1940, page 322.

L. F. Wooley: "Immediate Circulatory and Respiratory Effects of Convulsive Shock (Curare-Protected Metrazol and Electric Shock)", *The Journal of Nervous and Mental Diseases*, Volume C, July, 1944, page 1.

Reviews.

ANÆSTHESIA.

"ANESTHESIA IN GENERAL PRACTICE", by Dr. Stuart C. Cullen, is published by The Year Book Publishers of Chicago.[1] The general appearance of the book is fresh and attractive, it is well bound, well printed on good paper, and is in many ways a reminder that the war is over and that books of quality may once again reach our hands.

The claim made in the title is very modest, for the book reveals the profound knowledge and very wide experience of the author and covers technique beyond the resources of general practice. The method of presentation is much after the American pattern. Diagrams and drawings are used to amplify the usual illustration plates, many of these being reproductions. The subdivision into chapters and the general layout make for clear presentation and ease in reading. A good bibliography accompanies each chapter.

The substance is essentially sound and those chapters dealing with general principles are equal to anything previously published. There is a pleasing lack of dogmatic detail and complicated technique and the author displays a delightful directness and firm insistence on basic principles. An isolated sentence is seldom sufficient evidence on which to form an opinion or pass judgement, but the following may serve to convey something of this author's method. "It is an interesting, albeit an alarming, paradox that although individuals are given police protection for the maintenance of their airway (death by strangulation is murder), many persons are subjected to strangulation in hospital operating rooms under the guise of anesthesia. It is a conservative estimate that 90 per cent. of the deaths occurring in patients under anesthesia are due to improper management of the airway." This chapter called "Airway" is a contribution to the literature of anæsthesia which alone would justify publication of this book, were any justification needed.

The chapter on agents gives much valuable information about the usual list of anæsthetic drugs used. It includes tests for the purity of ethyl ether and other useful knowledge which has not been presented previously in this concise and practical form. About chloroform: "Its usefulness is limited to those rare instances in which no other non-inflammable agent is suitable." "There is no justification for the use of ethyl chloride for anesthetic purposes". These are statements which might provoke heated argument in some parts of the world.

The "standard technic" for spinal analgesia, described in the chapter devoted to this subject, is vague and falls far below the standard set by the earlier chapters.

The chapter covering regional infiltration and topical analgesia is excellent. A series of humorous pen drawings illustrates "Procaine" reactions and their treatment. Technique is described for block of cervical plexus, brachial plexus and others of the more useful and commonly needed nerve blocks.

The chapters devoted to shock, oxygen want and pre-anæsthetic and post-anæsthetic care of the patient show clearly the responsibilities and duties now recognized as those of the anæsthetist. Moon's work on shock is the basis of the chapter on the recognition and treatment of this condition. The subject is dealt with very well in the few pages devoted to it and sound principles and some details of treatment are clearly enunciated.

The very important subject of oxygen therapy is dealt with fully under the headings of "Signs of Oxygen Want", "Physiology of Oxygen Transport", "Types of Oxygen Want" and "Methods of Administration". Like the chapter on airway, this has a certain originality about it and offers an excellent presentation of the subject, making quite clear its paramount importance to the anæsthetist.

"Anesthesia in General Practice" is a valuable addition to the literature of anæsthesia. Anæsthetists of all grades of experience and aspiration would gain knowledge and pleasure from reading it before placing it on their shelves for further reference.

[1] Anesthesia in General Practice", by Stuart C. Cullen, M.D.; 1946. Chicago: The Year Book Publishers, Inc. 8¼" × 5¼", pp. 260, with many illustrations. Price: 28s.

GYNÆCOLOGICAL ENDOCRINOLOGY.

THE excellent little book "Gynæcological Endocrinology" by Bishop should be very valuable to the busy practitioner.[1] It will, as the author states in the preface, "dispel the chaos which has been created in their minds by the predilection of pharmaceutical business houses to give proprietary names to endocrine preparations". It is a small book and can be perused and understood by the practitioner in a comparatively short time. This fact alone should do much to counteract the tendency to acquire knowledge of endocrinological therapy from blotting-pad literature.

The author presents an excellent chapter on "Sex Hormones and Administration". This chapter gives a concise description of the hormones and very valuable information regarding their methods of administraton and dosage. In the chapter "Amenorrhœa" the author gives a timely warning about the disappointments in the treatment of this condition by the sex hormones. A very sound and useful chapter is given on "Excessive Bleeding". The discussion in this chapter on androgen therapy should be very useful to the practitioner, as also should be the part dealing with *metropathia hæmorrhagica*. The value of hormone therapy is shown very clearly in regard to vaginal blood losses. A further useful chapter deals with the "Endocrinology of Pregnancy". An appendix of commercial preparations including their cost is also given and the list appears to be comprehensive.

[1] "Gynæcological Endocrinology for the Practitioner", by P. M. F. Bishop, D.M. (Oxon.); 1946. Edinburgh: E. and S. Livingstone Limited. 7½" × 5", pp. 132, with illustrations. Price: 7s. 6d.

The Medical Journal of Australia

SATURDAY, JANUARY 4, 1947.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: initials of author, surname of author, full title of article, name of journal, volume, full date (month, day and year), number of the first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

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THE PROBLEM OF THE DOMESTIC STAFF IN HOSPITALS.

DURING the last few years numbers of hospitals in all States of the Commonwealth have been compelled to close down on the use of certain beds and many, particularly among private hospitals, have been compelled to close their doors because those in control have been unable to secure sufficient nurses and domestic workers. The problem is largely but not entirely the result of wartime conditions. Even before the war the recruiting of young women as trainees in nursing schools associated with hospitals was becoming increasingly difficult and the same was true of efforts to obtain women for the domestic staffs. The problems of nursing and nursing trainees were discussed in these pages not so long ago, but the only reference to the difficulties of obtaining domestic staff for hospitals has been made in reports of meetings of the Federal Council during the last year or two. Domestic staffs are just as necessary to the running of hospitals as are nursing and even medical staffs. Without medical or nursing staff a hospital would become a hostel; without a domestic staff a hospital cannot be run at all, unless members of the nursing staff, as they sometimes do, attempt the impossible by trying to carry out domestic duties as well as their own professional work. The problem of the domestic staff is not peculiar to Australia; it exists in Great Britain, and we may well assume, in other countries as well. Inquiries have been made and suggestions have been put forward in regard to conditions of work, remuneration and certain psychological considerations. Some of these inquiries have been valuable and our present object is to draw attention to a report that has been prepared by the King Edward's Hospital Fund for London at the request of the Factory and Welfare Advisory Board of the Ministry of Labour and National Service.[1] It is necessary first of all, however, to state that the underlying cause of the trouble is to be found in the general post-war economy. In February, 1946, the Prime Minister of Great Britain declared that the nation was faced with a shortage of manpower. It was necessary, he said, to see that manpower was used to the best advantage, and that meant a changed attitude of mind. The attitude of mind which had to be changed was the result of the surplus labour of the pre-war period and of the large amount of unemployment then existent. If there was a labour shortage, it was necessary to use what was available to the best advantage and also to use science to save labour. *The Times* of May 31, 1946, quoted a government white paper's statement that the total manpower available was insufficient to meet in full all the demands of industry. The same newspaper on June 20, 1946, pointed out that the carrying into effect of the Government's economic plans depended upon a total working force of twenty millions in 1947, and that success would not be possible unless there were retained in the labour market up to half a million more women than before the war. At that time there were in the labour market 680,000 women in excess of pre-war numbers. In spite of this excess of numbers the domestic staff problem in the hospitals of Great Britain is presenting the greatest difficulties. In these circumstances hospitals must find a solution that will enable them to stand up to the competition in the rest of the labour market. What is true of Britain in this regard is equally true of Australia.

When the Factory and Welfare Advisory Board of the Ministry of Labour and National Service asked the King Edward's Hospital Fund for London to examine matters connected with the employment of domestic staff in hospitals, it pointed out that the fact had to be faced that hospital domestic work was at that time an unpopular occupation, particularly among women used to factory conditions. A small committee was set up under the chairmanship of the Right Honourable Malcolm McCorquodale. The committee consulted among others hospital administrators, matrons and personnel managers in industry. It inquired into such matters as the causes to which the hospitals attributed the shortage, the arrangements for the engagement, supervision, training and general welfare of the domestic staff, the labour-saving equipment used, the accommodation and amenities provided and the difficulties in the way of effecting improvements. No attempt was made to compile statistics on shortage of staff, but evidence was obtained from sixty hospitals of all sizes and all but five reported a serious shortage of domestic staff. The hospitals were relatively well placed in regard to town amenities and many were able to offer good conditions. This is not true of all the hospitals in the country and the conclusion is drawn that therefore the whole hospital system must be gravely affected by the shortage. This is known to be the case, and "the situation is in fact one of emergency". Quoting the words of the Prime Minister, which have already been referred to, the committee states that it cannot evade the unpalatable truth that it is insufficient to carry on in the hope that the labour situation will become easier and that the first hint of unemployment will bring the recruits that the hospitals have been unable to find. The following pertinent question is asked and it may be asked in Australia as well: "Have the domestic arrangements and methods been adjusted to meet changed conditions, or have they persisted without revision since the days when

[1] "Recommendations on the Employment of Domestic Staff in Hospitals"; published for King Edward's Hospital Fund for London by George Barber and Son, Limited, Furnival Street, London, E.C.4. 8½" × 5½", pp. 34. Price: 9d. net, post free.

domestic labour was cheap and abundant?" There is no reason to expect a "return to plenty" and it is necessary to cut the garment according to the cloth. "As a long-term policy, this implies a radical adjustment rather than a perpetuation of the present attempts by hospitals to carry on as best they may."

Some of the recommendations of the committee are concerned with the introduction of workers from Europe; as they have no possible bearing on the present Australian conditions they may be ignored. Little mention is made of remuneration except that there have recently been promulgated national minimum rates of pay and standard conditions of service for staff in hospitals and allied institutions. Australia has its standards of payment for work in hospitals. The point about these standards is that they are minimum rates. The English committee is quite right in its view that individual hospitals should have freedom to offer as much more as may be deemed necessary to overcome special disadvantages. The disadvantages named are remoteness from a town and old and inconvenient buildings. To these might be added the disadvantages or the unpleasantness associated with certain types of work. For example, in certain mental hospitals both the nursing and domestic staffs are called upon to undertake duties for patients whose condition makes their surroundings anything but pleasant. A discrimination in favour of members of the staff who deal with these surroundings, if applied wisely, should do something towards the promotion of harmony and peace. The suggestion is made that good payment may improve the type of employee on a domestic staff. This presumably means a type with a higher grade of intelligence or of physical strength; it may mean a "more stable" type. Good physique is necessary in the domestic work of a hospital, but in every institution surely work can be found which can be efficiently done by one or more physically handicapped persons. The intelligence of the average man or woman in this country is by no means low, and stability is as much the result of environment as of innate quality. This brings us to one of the important recommendations—for the appointment of a domestic supervisor or welfare officer. It will be quite easy to neglect the health of the domestic staff of a hospital, the members being something like the shoemaker's wife who is worse shod than her neighbours. Obviously the appointment of a supervisor and welfare officer will depend on the size of the staff, but since such an officer is successful in ordinary industrial concerns, nothing but good could come from such an appointment in a hospital. The committee does not recommend that the domestic supervisor should be regarded as head of a separate department and not responsible to the matron. The matron must have the ultimate responsibility for the domestic staff. Such matters as labour-saving devices and their use, hours of duty and arrangement of shifts, accommodation and amenities, and even pensions are mentioned. These may all be summed up as coming within the ambit of industrial medicine. This is a subject which has been discussed in these pages on many occasions. For practical purposes the running of the domestic side of a hospital should be regarded as similar to the running of an industrial concern. With so many doctors about the place a hospital should set an example as a centre of industry. But again we think of the shoemaker's wife or perhaps of the doctor's children whose adenoids are so long unremoved because the father is the father and not the doctor when he sees his children every day. Two final suggestions may be mentioned. One is the possible employment of male domestic orderlies. This has been done with success at the Women's Hospital, Brisbane, where returned soldiers are doing in a competent way work that was formerly done by wardsmaids. The other suggestion is the introduction, as soon as regulations permit, of an attractive and practical uniform for hospital workers. Whether this would appeal to Australians from any point of view other than that of economy, is doubtful.

This short review of some aspects of the London report shows that there are still steps that may be taken in this all-important question. Too often the Australian State Minister faced with this problem and with suggestions to solve it, makes a promise which he promptly forgets. *The Times* made a statement on the subject of women in industry which, though perhaps debatable in one respect, contains much truth and may therefore be used to close this discussion:

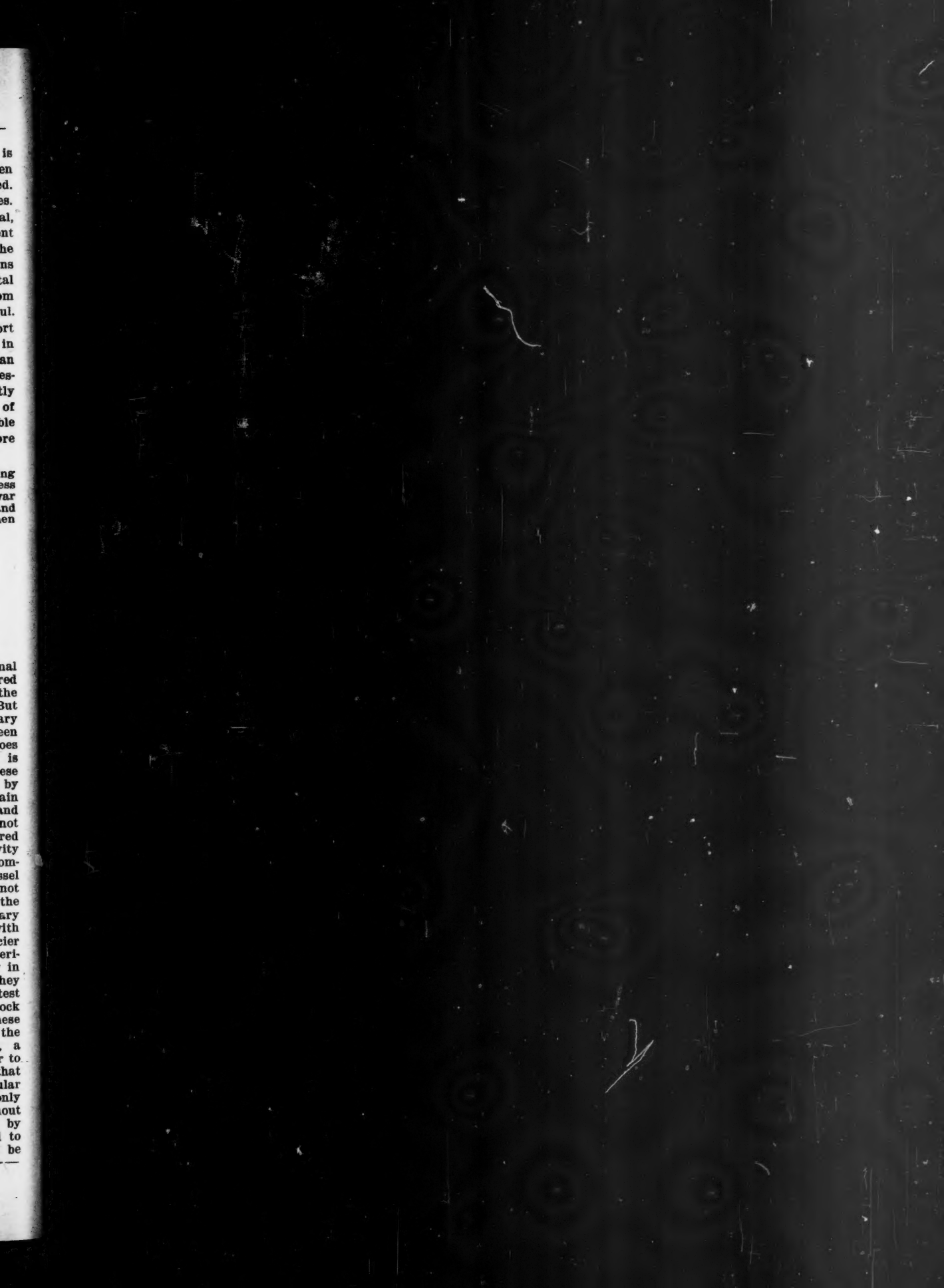
> It is likely that industry will not succeed in retaining all the women who could be usefully employed unless it is prepared to learn some of the lessons of the war and in particular to reconsider its attitude to the demand for equal pay, to the part-time employment of women and other kindred topics.

Current Comment.

PERICORONARY NEURECTOMY IN CORONARY DISEASE.

FOR a number of years the surgical relief of anginal pain has been closely studied. At first sceptics feared that the removal of Nature's warning might subject the patients to special hazards through unwise exertion. But all persons who have suffered an occlusion of a coronary artery do not have anginal pain. Further, it has been observed that more than one overpowering sensation does not arise in consciousness simultaneously, and there is another type of discomfort which is perceived by all these patients if their attention is not completely diverted by pain, namely, breathlessness. Indeed, since anginal pain needs two factors for its production, cardiac ischæmia and sensitivity of the afferent nervous mechanism, it cannot be said that a patient is any better off because the red stop-light of pain warns his body that its traffic activity must be temporarily restrained. When ischæmia is accompanied by pain is there constriction of a coronary vessel and, if so, is it greater or less than in persons not suffering pain? It surely must be conceded that the surgeon who tries to relieve anginal pain due to coronary disease should reinforce his humanitarian arguments with others that have some physiological basis. Mercier Fauteux and Orvar Swenson have published an experimental study on the value of pericoronary neurectomy in coronary disease which is of considerable interest.[1] They maintain that for any surgical procedure to be of greatest value it should improve the coronary circulation, block vasomotor reactions and eradicate anginal pains. These requirements at once stamp the various operations on the sympathetic nervous system as doubtfully efficient, a judgement which time seems to be confirming. In order to devise a satisfactory procedure it seemed to Fauteux that such an operation should be carried out on the vascular system of the heart itself and should include not only interruption of the reflex nervous paths there, without interfering with the function of other organs supplied by the same sympathetic trunks, but also steps designed to improve local circulation. The latter objective might be

[1] *Archives of Surgery*, August, 1946.



attained by ligation of coronary veins. Extensive experimental studies had previously been carried out by this author which supported the validity of these ideas, which he pursued in collaboration in the present communication.

It is claimed that ligation of coronary veins has been found in this work to encourage collateral circulation and that in human patients who have had the great cardiac vein tied beneficial results have been seen. In the present study dogs were used for the experimental work, one group having been prepared by previous cardiac neurectomy. Both the prepared and the control series were then subjected to ligation of the left coronary artery. The ligature was left loose and brought out to the surface through a fine cannula, so that it could be tightened by traction. Observation of the animals showed whether the procedure caused pain or not, and this could be satisfactorily done without subjecting them to undue discomfort. The interruption of the nervous paths included resection of all the branches emerging from the space between the aorta and the pulmonary artery at the base of the heart, and also the removal of the epicardial tissue over the left coronary artery from its origin to a little below its bifurcation. Electrocardiographic studies were carried out on both groups of animals. One of the authors performed all the operations and the other carried out all the tests. The results obtained encouraged them to extend their work to the human subject. In all, nine patients have been operated on, and although sufficient time has not yet elapsed for evaluation of the procedure, at least it is established that it can be done without undue risk and the first two patients of the series are much improved in the matter of comfort. One patient is now working successfully; the others cannot be discussed, as details are not yet available. Fauteux and Swenson admit that it is too early to reach any final judgement about the value of this operation, but they claim that both the experimental and the clinical results are sufficiently encouraging to warrant its further trial.

THE EFFECTS OF ACUTE ANHYDRÆMIA.

MUCH has been written about shock and in particular about the immediate effects of burns. Work has been referred to in these pages which has demonstrated the importance of infection as a factor in experimental shock following injury. In burns it is hard to exclude this factor also, but there is ample evidence that the loss of body fluid alone is of great importance. This is further emphasized in an experimental study by G. R. Cameron, F. Burgess and V. Trenwith.[1] They remark that there is general agreement as to the domination of this factor of fluid loss in the early symptoms following burns, but that some of the later features are not so convincingly explained. They have used the simple technique of introducing large amounts of hypertonic solutions of salt or glucose into the subcutaneous tissues of rabbits and goats. This was usually done under light "Nembutal" anæsthesia, and blood investigations were carried out at regular intervals. The animals were given unlimited food, but no water afterwards, and some were killed after periods of six, twenty-four and forty-eight hours for pathological study. Blood pressure estimations were also made. Goats can tolerate large amounts of glucose, up to twenty millilitres of 60% glucose per kilogram of body weight. Rabbits are not always so tolerant, but the results for the two species are much the same. Within a few hours the hæmoglobin percentage, the red cell count and the hæmatocrit reading rise to a peak which usually occurs between twelve and twenty hours. As œdema appears at the site of the injection, the plasma volume falls. The serum protein, after a slight rise, assumes a stabilized figure. These disturbances generally have subsided after forty-eight hours. During this period there has obviously been little protein lost from the blood, and therefore little capillary damage can have been caused such as might allow an increase in permeability. It is presumed that various tissues have been responsible for compensatory withdrawal of fluid, and the condition is thus one of uncomplicated anhydræmia. At the same time well-defined clinical changes are observed. The animals huddle up as if cold, are weak, particularly in the hind limbs, the respiratory rate increases, and muscular spasms may occur. At this stage some susceptible animals like rabbits may succumb. There seems reason to believe that a fatal termination must be due to circulatory collapse, and this is supported by the progressive fall in blood pressure which occurs. Pathological examination of the tissues and organs at this stage shows little but œdema at the site of the injection, and infection is rare. Widespread congestion of the blood vessels of the body is seen, however, even as early as six hours after the onset, involving the lungs, liver, kidneys and intestine. A few petechiæ may be seen in the heart. These signs are more in evidence after twenty-four hours. They are in fact consistent with the great constriction of peripheral arterioles. These experiments avoid the complicating factor of necrotic tissue, such as inevitably occur in burns, and yet the clinical picture and the pathological findings are strikingly similar. It is, as the authors point out, not sufficient to regard the explanation of acute anhydræmia as satisfactory in understanding all the symptoms, for we cannot say with certainty why the effects of anhydræmia should be so severe. The suggestion that anoxæmia can explain the seriousness of fluid loss seems reasonable, and the greatly decreased flow of blood through the extremities would surely affect the circulation through the internal organs to an unknown degree. Investigation of tissue respiration, as Cameron and his co-workers suggest, might yield valuable information. Acute anhydræmia appears to explain the urgent early signs and symptoms following burns, and as these authors practically remark, this theory is justified as a working hypothesis.

[1] *The Journal of Pathology and Bacteriology*, April, 1946.

THE STAFFING OF HOSPITALS IN WESTERN AUSTRALIA.

IN view of the leading article in this week's issue on the problem of the domestic staffs of hospitals, it is of interest to note an effort which has been made to secure nurses for the hospitals of Western Australia. In *The West Australian* of December 5, 1946, is a short account of a direct approach that has been made to eight hundred nurses who are believed to be engaged in other than hospital work. The Under-Secretary for Health, in announcing the sending of a letter to the nurses, referred to the position as an emergency, the seriousness of which could not be over-emphasized. In the letter attention was drawn to the improved wages and conditions now available for work in hospitals. A new award, superior to the old award, had been made and weekly hours had been reduced to 44. The actual appeal is as follows: "This appeal is based not only upon the needs of the sick for whose relief you have been trained, and whom no one but you and those like you can assist, but also upon the generous rewards which nursing offers. No longer can it be suggested that the nursing profession is neglected." It is admitted that many of the women to whom this appeal is directed are unable to return to the work of nursing, having taken on other responsibilities, which have a prior claim on them. This appeal is a good idea. That it has been made is a tribute to the women of Western Australia. It is to be hoped that the Western Australian Government's belief in their sense of responsibility and public spirit will be justified. Whether this appeal succeeds or not, a drive should be made to secure recruits for the hospital training schools. As has so often been pointed out, it is not sufficient to promise short hours and good wages. The living accommodation of nurses needs an overhaul and the attitude of matrons to the recruits must in many cases be completely altered. After all, if a young woman is fit to have the care of sick persons, she should not be treated like a girl in a boarding school; the probationer nurse has the same right to a normal social life in her own time as any other woman.

Abstracts from Medical Literature.

OPHTHALMOLOGY.

Influence of Local Antiseptics on Regeneration of Corneal Epithelium of Rabbits.

J. G. BELLOWS (*Archives of Ophthalmology*, July, 1946) investigated the effect of antiseptics on regeneration of corneal epithelium. The corneæ of rabbits were denuded of epithelium by first instilling cocaine solution and then rubbing with gauze. Agents studied were instilled into the left eye three times a day, while the right or control eye received a similar amount of isotonic solution of sodium chloride. Solutions of the following were investigated: mild silver protein (10% aqueous), zinc sulphate (0·5% aqueous), marbromin (2% aqueous), phemerol chloride (1:2,500 concentration in 2% boric acid solution), mercuric oxycyanide (1:5,000 aqueous), "Metaphen" (1:2,500 aqueous), "Merthiolate" (1:2,500 aqueous), acriflavine (1:1,000 aqueous), "Zephiran Chloride" (1:3,000 aqueous), penicillin (one millilitre containing 2,500 Oxford units) and sodium sulphathiazole (2% aqueous). The author was able to conclude that the local antiseptics ordinarily employed in ocular therapeutics had considerable delaying effect on the healing process of corneal epithelium of rabbits. In most instances these drugs caused a permanent opacity of the cornea. Phemerol chloride (1:5,000 concentration in 2% boric acid solution) delayed healing only slightly and produced no permanent alterations in the cornea. Sodium sulphathiazole in 2% aqueous solution, and penicillin in a concentration in which one millilitre contained 2,500 Oxford units, neither delayed the regeneration of epithelial covering nor produced corneal opacities. The author recommends that in the treatment of corneal injuries, in which the possibility of infection is great, the aqueous solution of sodium sulphathiazole or penicillin may be used.

Use of Diisopropyl Fluorophosphate ("DFP") in Treatment of Glaucoma.

I. H. LEOPOLD AND J. H. COMROE (*Archives of Ophthalmology*, July, 1946) studied the effect of "DFP" on glaucoma, having previously studied its effects on the normal eye. "DFP" has a prolonged miotic effect in normal men and animals; the miosis may be accompanied by spasm of accommodation and ciliary pain. These effects are due to the inactivation of cholinesterase and not to direct action on iris and ciliary muscle. The reaction of "DFP" is at least five and a half times as potent and much more persistent than physostigmine. "DFP" can also overcome the effects of atropine and homatropine on pupil and ciliary muscle. Finally "DFP" resembles physostigmine in its influence on the intraocular tension of normal human eyes, differing, however, in that its effect is much more prolonged. In occasional normal human eyes a rise in intraocular tension persists for several days after one local application of very dilute preparations of "DFP". The authors treated 78 glaucomatous eyes in 52 patients during a period of six months. Only in eyes in which tension was maintained at or below 30 millimetres of mercury, and in which no loss of visual fields occurred, was the tension considered controlled. "DFP" was used in 0·05%, 0·1% and 0·2% concentration in oil. In only 43·7% of eyes affected by chronic simple glaucoma was pilocarpine or physostigmine, or a combination of both, successful in controlling the intraocular tension. Of the same eyes, "DFP" was successful in keeping the tension below 30 millimetres of mercury in 89·5%. Of eyes in which glaucoma developed after cataract extraction, pilocarpine or physostigmine, or a combination of both, was successful in lowering intraocular tension below 30 millimetres of mercury in only 40%, whereas "DFP" was successful in 100%. Administration of "DFP" may be required only once a day or even once a week. "DFP" has several untoward and undesirable ocular effects—namely, visual blurring, brow ache and eye ache, spasm of accommodation and pericorneal injection.

Early Ocular Manifestations in the Laurence-Moon-Biedl Syndrome.

DONALD LYLE (*American Journal of Ophthalmology*, August, 1946) describes three cases of the Laurence-Moon-Biedl syndrome, and discusses the early ocular signs. The syndrome consists of obesity, hypogenitalism, mental retardation, polydactyly and retinal degeneration. The subjective symptom is loss of central vision not correctable with glasses. Early visual field studies reveal an expanding central scotoma; peripheral concentive constriction gradually develops. Ophthalmoscopic examination may reveal no abnormality at first. White or pigmented macular spots or stippling appear usually in the early stage. Later the periphery of the retina begins to show atrophy, and finally pigment appears. With the peripheral changes, the retinal vessels become attenuated, and pallor is seen at the disk. The resemblance to Leber's hereditary optic atrophy and to various types of cerebro-macular degeneration with central scotomata, loss of vision and cerebral symptoms is remarkable in the early stages of these two conditions. In later stages, the pigmentary degeneration may be confused with *retinitis pigmentosa* by the observer who fails to take a detailed history and to make a complete examination in order to reveal the other components of the syndrome.

Exophthalmos Caused by Eosinophilic Granuloma of Bones.

M. WHEELER (*American Journal of Ophthalmology*, August, 1946) describes the case of a young man, aged thirty-four years, who had a history of swelling of the right upper eyelid of five weeks' duration, followed by pain behind the eye. The swelling varied. Exophthalmos of the right eye of two millimetres was present, the globe being displaced downward about four millimetres. X-ray examination revealed a fairly circular defect through the roof of the right orbit. At operation a tumour was located in the region of the lachrymal gland. It was flattened and firm, lying above the gland and extending back about three centimetres into the orbit along its supero-lateral wall. The mass contained soft, partly necrotic granulation tissue, which was removed with a curette used as a spoon. Nine months after operation one millimetre of exophthalmos was present, and X-ray examination revealed that the inferior portion of the lesion of the roof of the orbit was healed and the defect largely filled in. On examination the necrotic granulation tissue was found to contain large numbers of histiocytes, many of which showed evidence of phagocytic activity, and occasional large multinuclear giant cells. There were also numerous eosinophilic and neutrophilic leucocytes and many clumps of mononuclear cells taking an eosinophilic stain.

Exophthalmic Ophthalmoplegia and its Relation to Thyreotoxicosis.

IN a review of relevant literature, Ida Mann (*American Journal of Ophthalmology*, June, 1946) elucidates the experimental findings with regard to exophthalmic ophthalmoplegia and thyreotoxicosis in guinea-pigs and attempts to correlate these findings with those found in human beings. Both exophthalmos and proptosis can be produced experimentally in many animals by agents which stimulate smooth muscle; both are transient, disappearing when the animal is anæsthetized or killed, and are prevented by section of the cervical sympathetic trunk. These experiments, while explaining lid retraction and the staring look of thyreotoxic patients, do not explain proptosis, as proptosis developed in a patient with paralysis of the cervical sympathetic trunk. Smelser pointed out that extracts of the anterior lobe of the ox pituitary produced true proptosis in guinea-pigs after thyreoidectomy. In these animals there is an increase in orbital contents—100% in the fat, 40% in the dorsal lachrymal gland and 22% in the extrinsic muscles. Connective tissue hyperplasia and œdema will be found to account for the increase in fatty tissues; œdema and round-cell infiltration account for increase in the muscles. This connective tissue hyperplasia and water retention involves other body fats of the guinea-pig. These effects are due to excess secretion of the anterior lobe of the pituitary. The effects of excess thyroxine in guinea-pigs are different—namely, loss of weight, and finally enophthalmos from absorption of orbital fat. Marine and Rosen consider that sympathetic stimulants which produce lid retraction and transient exophthalmos from contraction of smooth muscle act more readily in the presence of excess thyroxine. Mann states that there are three sets of eye signs: signs of overaction of unstriped muscle, signs of weakness of striped muscle and signs of increase in bulk in orbital and lid tissues. General changes due to excess or deficiency of thyroxine may also complicate the picture. In addition there is the possible action of the central nervous system acting through hypothalamic structures as the stimulant or depressor of the pituitary. Mulvany considers that two completely distinct conditions exist, one due to excess thyroxine, and the other due to excess of anterior pituitary hormone. The first he calls thyreotoxic ophthalmoplegia; in it are observed weakness of extraocular muscles, retraction of the upper lid, exophthalmos and weakness of muscle action, but no increase in orbital content. The second he calls thyreotropic exophthalmos; in it anterior pituitary hormone produces structural changes in the striped muscles of the orbit as well as a true increase in volume of the orbital contents, with œdema of the lids, orbital

contents and conjunctiva. Ophthalmoplegia and proptosis result. The author divides the clinical cases into the following three groups: Group I. Primary deficiency of thyroxine with compensatory excess of thyreotropic secretion. Group II: Primary excess of thyroxine as an initial symptom, followed by thyreoid atrophy or removal, and replaced by an excess of thyreotropic hormone. Group III: Excess thyroxine and excess thyreotropic hormone arising simultaneously. A full description of representative cases is given. The author concludes that signs of excess thyroxine are loss of weight, rapid pulse, raised basal metabolic rate, soft, moist skin, lid retraction and lid lag; whereas the signs of an excess of anterior pituitary thyreotropic hormone consist of orbital, lid and conjunctival œdema and infiltration, and hence proptosis, ophthalmoplegia, fundus changes, lid œdema, chemosis, and eversion of the conjunctiva, all of which may or may not be associated with deficiency of thyroxine. This deficiency will manifest itself by producing a low basal metabolic rate, a gain in weight, thick, coarse skin and a slow pulse.

OTO-RHINO-LARYNGOLOGY.

Irradiation of the Eustachian Tube.

E. P. FOWLER (*Archives of Otolaryngology*, January, 1946) points out that there is considerable difference of opinion about the amount of lymphoid tissue which is normally present in and about the Eustachian tube. This has caused controversy regarding the theoretical value of different types of radiation. For this and other reasons various types of filtration have been used for radon and radium, while some have suggested that high voltage X-ray therapy should be employed. When excess of lymphoid tissue is seen about the *torus tubarius* and there is improper function of the tube, it has been assumed that the lymphoid tissue is responsible. The best basis for this belief has been the clinical observation that irradiation of the mouth of the tube reduces the lymphoid tissue, and this is usually followed by improvement in the function of the tube. In the study of the aerootitis problem in flying personnel it has been possible to examine sections of the Eustachian tubes from airmen killed in action. This study suggests that lymphoid tissue is rarely abundant enough to block the tube except at the nasopharyngeal orifice, precisely where it is easiest to attack the tissue with radium. In some specimens lymphoid tissue covered the torus, yet many of these airmen had never had aerootitis. It is suggested that it is the addition of mucus to the narrowed tubal ostium which causes blockage. Sixteen post-mortem specimens were cut and stained so as to allow analysis of the microscopic appearance of the entire length of the tube. A low-grade salpingitis thought to be due to climatic influence was evident in most and slight round cell infiltration was one result of this. In more advanced inflammation some masses of lymphoid tissue with germinal centres were evident, the lymphoid tissue appearing to push through the columnar epithelium. Lymphoid masses were rare, except near the pharyngeal orifice, but in the presence of chronic infection such tissue was evident up to and beyond the isthmus. Of eighty airmen treated by irradiation for aerootitis, forty-six were known to have returned to full flying duty after two or more treatments. It is thought that in those who were unrelieved lymphoid tissue may have been far up the Eustachian tubes. The possibility of psychic effect from radium treatment was eliminated by treatment of a control group with dummy applicators. Only one of the control group of seventeen returned to duty without symptoms. Thirteen of the group of seventeen who had active radium returned to full flying duty. The author used two types of applicators, one containing 75 millicuries of radon and filtered with 0·65 millimetre of platinum, the other radium sulphate 50 milligrammes through walls of 0·5 millimetre of platinum. The dosages from these two applicators and that from the radium applicator originally used by Crowe which had 1·0 millimetre of brass filtration are compared. One millimetre of brass filters out all but 8% of β radiation. Crowe used this applicator for only two to three treatments, giving 33 milligramme hours at intervals of three weeks. In adults it is unusual to get the same result with radium and 0·5 millimetre platinum filtration unless four to six treatments of 50 milligramme hours are given at intervals of four weeks. A more recently employed applicator contains 50 milligrammes of radium salt and filtration of 0·3 millimetre of "Monel" metal. These are used for six minutes and forty seconds, in contrast with the hour used with the 0·5 millimetre of platinum, and it has been shown by ionization experiments that the new applicator delivers at 1·0 millimetre depth seven times as much radiation as the other, and 75% of this is β radiation in contrast with almost pure γ radiation when filtration of 0·5 millimetre of platinum is used and only 8% of β rays with 1·0 millimetre of brass. With the "Monel" metal filtration there is a heavy dose at the surface, but practically none in the deeper tissues. The brass applicator gives a relatively heavy dose at the surface and a light dose more peripherally along the Eustachian tube. It is thought that in some resistant cases applicators emitting the more deeply penetrating γ rays may be more useful. Since the effect of β rays is less understood, any increase in dosage time must be very cautiously undertaken.

Cancer of the Larynx: Results of Concentration Radiotherapy.

MAX CUTLER (*Archives of Otolaryngology*, April, 1946) reports on 118 consecutive patients suffering from cancer of the larynx who were treated by irradiation at the Chicago Tumour Institute, the most recent being treated three years ago. The main conclusions are based on the results observed in a group of 47 cases with a minimum observation period of five years. The basic principle of concentration radiotherapy is that large daily doses are given over a comparatively short period. With certain exceptions, the dose is increased every day and the size of the portal is diminished. The commonly employed Coutard method of divided daily doses given through two lateral fields, so that a total of 6,000*r* to 7,000*r* is given over a period of four to seven weeks, fails to cure the most resistant types. In concentration radiotherapy 6,000*r* to 6,500*r* are administered in eighteen days to one field. The total dose is sufficient to cause an epithelial and usually an epidermal reaction. A problem was how to adjust the various factors to render the treatment reasonably safe. Most of the patients were treated with 400 kilovolt rays, the intensity varying between 5*r* and 10*r* per minute. Usually one lateral field is used. The field is reduced gradually as the daily dose is increased, so as to reach the central remnant of the growth. Great precision is necessary; the apparatus calls for special light-centering devices, and the patient is securely immobilized during treatment. The time of exposure is influenced by the observation that the more resistant a growth, the shorter must be the time of treatment and the larger the daily dose. Treatment periods of four to twenty-two days have been tried, and the matter of the optimal period is not yet settled. One technique of an eleven-day period gave excellent results, but proved too intense for certain patients. This led to an increase to eighteen days, and so far there have been no untoward effects from this technique. Details of two Röntgen ray techniques in general use at the institute are quoted, as well as the most effective telecurie-therapy technique, for which ten grammes of radium have been available. Statistical records reveal that in the series of 47 patients, comprising 17 whose cords were movable or partly fixed and 30 with advanced cancer whose cords were fixed, 18 have survived for five years without recurrence. Of this group 31 had extrinsic inoperable growths and eight survived, and of seven otherwise suitable for laryngofissure, five have survived. In the group of 118 cases, 43 or 39% have survived and are free of recurrences after an interval of three years. The question is considered of choice between operation or irradiation in early laryngeal carcinoma amenable to laryngofissure. While the high rate of cure with surgical treatment in suitable early cases remains impressive, it is stressed that it seems that the results of irradiation in these cases are at least as good as those after operation, with the added advantage of retention of a normal voice. When the lesion has reached the posterior extremity of the cord without impairing mobility, laryngofissure is contra-indicated, and irradiation is to be preferred to laryngectomy. It is considered hazardous to draw conclusions regarding radiosensitivity or operability from the histological structure of a biopsy specimen except in a general way. It is a fallacy that squamous carcinoma has been held to be insensitive to irradiation; it has been found sensitive to maximum radiotherapy. Experience has indicated that papillary lesions are radiosensitive and infiltrating lesions relatively resistant. Cancers arising in the vocal cords are usually sensitive only before infiltration of the underlying muscles. Carcinoma arising in the false cord or epiglottis is generally radiosensitive even in advanced stages. Mobility of the laryngeal structures generally indicates that the lesion is early, or if it is visibly advanced, that it is papillary and not infiltrating. From the point of view of radiotherapy, the latter type of lesion is considered to be sensitive and probably curable. It has been observed that any subsequently required radical surgical treatment is not seriously prejudiced by previous irradiation.

Bibliography of Scientific and Industrial Reports.[1]

THE RESULTS OF WAR-TIME RESEARCH.

During the war a great deal of research was carried out under the auspices of the Allied Governments. It has been decided to release for general use a large proportion of the results of this research, together with information taken with former enemy countries as a form of reparations. With this end in view, the United States Department of Commerce, through its Publication Board, is making a weekly issue of abstracts of reports in the form of a "Bibliography of Scientific and Industrial Reports". This bibliography is now being received in Australia, and relevant extracts are reproduced hereunder.

Copies of the original reports may be obtained in two ways: (a) Microfilm or photostat copies may be purchased from the United States through the Council for Scientific and Industrial Research Information Service. Those desiring to avail themselves of this service should send the Australian equivalent of the net quoted United States price to the Council for Scientific and Industrial Research Information Service, 425, St. Kilda Road, Melbourne, S.C.2, and quote the PB number, author's name, and the subject of the abstract. All other charges will be borne by the Council for Scientific and Industrial Research. (b) The following reports may be obtained in approved cases without cost on making application to the Secondary Industries Division of the Ministry of Post-War Reconstruction, Wentworth House, 203, Collins Street, Melbourne, C.1. Copies of these are available for reference in public libraries.

Further information on subjects covered in the reports and kindred subjects may be obtained by approaching the Council for Scientific and Industrial Research Information Service, the Secondary Industries Division of the Ministry of Post-War Reconstruction, or the Munitions Supply Laboratories (Technical Information Section), Maribyrnong, Victoria.

PB 19183. U.S. WAR DEPARTMENT. ARMY SERVICE FORCES. Operating procedures for industrial dispensaries. (Manual M210.) March, 1945. 30 pp. Price: Microfilm, 50c.; Photostat, $2.00.

This manual is presented as a guide to be followed in establishing and maintaining adequate medical service for employees in army-owned and army-operated industrial installations within the Army Service Forces. It is divided into the following sections: I. General Instructions; II. Industrial Hygiene Engineering Service; III. Relationship with Civilian Personnel Department; IV. Preventive Medicine Programme and Job Assignment; V. Emergency Medical or Surgical Care; VI. Employees Returning from Sick Leave; VII. Records and Reports; VIII. Industrial Dispensary Buildings; IX. Industrial Dispensary Supplies and Equipment. Floor plans and properly filled out standard forms are included.

PB 19031. U.S. WAR DEPARTMENT. MEDICAL CORPS. Hospital diets. (Tech. Manual 8-500.) March, 1945. 135 pp. Price: Mimeo, 4c.

This manual provides a guide for the arranging, ordering and preparing of diets not only for the average patient under usual conditions, but also for those requiring highly specialized consideration in their diets. It is also designed to serve as a reference guide for certain values, equivalents and percentages which of necessity must be considered in the preparation of all diets. Appendix lists, dietary reference, tables and numerous charts and other tables appear in the body of the manual.

PB 18957. U.S. WAR DEPARTMENT. OFFICE OF THE SURGEON GENERAL. COMMISSION ON AIR-BORNE INFECTIONS. T-13 oil emulsion for the application of oil to bedclothes and wearing apparel. April, 1945. 38 pp. Price: Microfilm, 50c.; Photostat, $3.00.

Preliminary studies in the application of oil to bedding to prevent the dissemination of dust, lint and bacteria led to the use of T-13 oil emulsion base which contains medicinal mineral oil and Triton Ne, a non-ionic wetting and emulsifying agent. This report is a final summary of data compiled by the Commission on Air-Borne Infections on the use of Triton oil emulsion (T-13) as a routine laundry procedure. It includes both laboratory and field studies made at the University of Chicago, Camp Carson, Colorado and Fort Bragg, North Carolina. The majority of the observations were made at Fort Bragg during the study, in collaboration with the Commission of Acute Respiratory Diseases, on the control of respiratory disease by oiling floors and bedclothes. The investigations were extended to include woollen and cotton wearing apparel and surgical operating room supplies. Detailed information is given regarding the application of the oil emulsion, the dust and bacteria holding properties of oiled textiles, and cost of the treatment.

PB 19228. U.S. WAR DEPARTMENT. SIGNAL CORPS. FORT MONMOUTH SIGNAL LABORATORY. Report on patch tests conducted at Forth Monmouth Signal Laboratory, March, 1945. May, 1945. 8 pp. Price: Microfilm, 50c.; Photostat, $1.00.

The results of patch tests showed that a fungus proofing wire impregnating material with 1% phenylmercuric salicylate and even with 0·2% phenylmercuric salicylate is a powerful skin irritant, and that a lacquer with 1% phenylmercuric salicylate is also. The remaining chemicals showed no such powerful primary irritating properties.

E.269. SMITH, BRIGADIER S. Developments in bacteriology and protection against malaria. (Dr. Habs, German malariologist.) (CIOS File No. XXVII-97.) June, 1945. 21 pp. (PB 538.)

Report of interrogations of several German doctors of medicine and/or chemistry on various medical subjects.

E.271. MCCARTHY, CAPTAIN CHARLES L., *et alii*. Miscellaneous interviews on medical practice and research in Germany. (CIOS File No. XXIX-13.) August, 1945. 26 pp. (PB 498.)

Interview covering research in malarial immunity, typhus vaccine and diagnosis, tuberculosis, skin and venereal diseases, neurology, psychiatry, gastro-enterology, orthopædics (mentioning an operation to give use to a handless arm), the use of skin resistance as an aid to diagnosis, the use of long nails inserted in the bone marrow channel in the treatment of fractures, and the isolation of a "male attractant" from the female silkworm.

E. 272. UHLE, COMMANDER CHARLES A. W. Martin Luther University, University of Halle. (CIOS File No. XXIX-1.) 4 pp. (PB 963.)

List of some of the personalities and work of the university—diphtheria, enzymes, fish protein and soap substitute specifically mentioned.

E. 270. RICE, J. B. Tropical medicines and other medical subjects in Germany. (CIOS File No. XXIX-35.) 1945. 24 pp. (PB 499.)

Deals with the methods of prevention and cure of malaria, trench fever, dysentery *et cetera* of a number of German experts. Information on the preparation of vaccines, special methods of dealing with bone features, and adaption to darkness are included.

PB 18631. U.S. ARMY TECHNICAL INTELLIGENCE CENTRE, TOKYO. Japanese medical equipment: hospital, shipboard. (Rept. 167.) January, 1946. 26 pp. Price: Microfilm, 50c.; Photostat, $2.00.

This shipboard hospital unit is apparently of recent type. It is excellently packed, relatively complete, and the instruments and medicinals are of the best that the Japanese produce. The hospital is well equipped to fulfill its purpose of giving field, not definitive, treatment to casualties prior to their evacuation to a main hospital installation. This unit contains a relatively large amount of plaster of Paris, but lacks the blood plasma, penicillin and sulpha drugs so prominent in corresponding United States Army installations. The unit is well balanced and well equipped to serve its purpose by Japanese medical standards. Fine photographs and a list of the miscellaneous items are attached.

PB 19291. ABRAMS, ADOLPH, *et alii*. The purification of type A botulinus toxin. October, 1944, to August, 1945. 37 pp. Price: Microfilm, 50c.; Photostat, $3.00.

This is a manuscript copy of a paper submitted for publication in *The Journal of Biological Chemistry*. A protein has been isolated from the *Clostridium botulinum* type A cultures and has been found to have the biological and immunological properties of the toxin. Methods, experimental data and discussion with tables, graphs, photomicrographs and bibliography make up this report.

PB 19293. BREWER, C. R., *et alii*. Application of nutritional studies for development of practical culture media for *Bacillus anthracis*. November, 1944, to March, 1945. 7 pp. Price: Microfilm, 50c.; Photostat, $1.00.

By the application of the results of previous nutritional studies, practical media designed specifically for growth of *Bacillus anthracis* have been developed. The report gives experimental data, results and discussion. Table is attached.

PB 19287. BREWER, C. R., *et alii*. The nutritional requirements of *Bacillus anthracis*. No date. 2 pp. Price: Microfilm, 50c.; Photostat, $1.00.

This appears to be an abstract of a report on an investigation to determine the nutritional requirements of *Bacillus anthracis*.

PB 19295. BREWER, C. R., *et alii*. Studies on the nutritional requirements of *Bacillus anthracis*. January, 1946. 20 pp. Price: Microfilm, 50c.; Photostat, $2.00.

This is a copy of a manuscript prepared for publication in the *Archives of Biochemistry*. The work presented is the

[1] Supplied by the Information Service of the Council for Scientific and Industrial Research.

result of studies on the nutritional requirements of *Bacillus anthracis*, Vollum strain, in a completely chemically defined medium. The necessity for the presence of thiamin was confirmed, and the stimulatory effects of uracil, adenine, guanine, phosphate, iron, magnesium, calcium and manganese were demonstrated. Tables, graphs and bibliography are attached.

PB 19288. BUEHLER, HENRY J., *et alii*. The amino acid composition of crystalline botulinus (type A) toxin. No date. 2 pp. Price: Microfilm, 50c.; Photostat, $1.00.

This report appears to be an abstract of a paper on this subject. In preliminary studies of the composition of this material the presence of fourteen amino acids has been determined. The toxin appears to be a complete protein in that it contains the ten essential amino acids necessary in animal nutrition. There is no suggestion of an unusual amino acid composition that might explain the extreme toxicity.

PB 19279. CORIELL, LEWIS L., *et alii*. The immunization of white rats against tularæmia. No date. 1 p. Price: Microfilm, 50c.; Photostat, $1.00.

This report appears to be an abstract of a paper on this subject. "The experimental immunization of white rats against tularæmia is described, using vaccines prepared from *Bacterium tularense* grown in embryonated chicken eggs, peptone, gelatin hydrolysate broth and dextrose cysteine blood agar."

PB 19290. CORIELL, LEWIS L., *et alii*. Observations on the cultivation of *Bacterium tularense* in embryonated eggs. No date. 1 p. Price: Microfilm, 50c.; Photostat, $1.00.

This report appears to be an abstract of a paper on this subject. The pathology of *Bacterium tularense* in the embryonated egg is described.

PB 19282. DOWNS, CORA M., *et alii*. The comparative susceptibility of various laboratory animals to *Bacterium tularense*. No date. 3 pp. Price: Microfilm, 50c.; Photostat, $1.00.

"The results on the various routes of injection of animals showed *Bacterium tularense* was infective by all routes tested and in general the animals were most susceptible when challenged subcutaneously or intraperitoneally. The susceptibility of the animals varied with the species; the dog, chicken and white rat being most resistant; the mouse, hamster, guinea-pig and rabbit being least resistant in the order named; and the cotton rat and monkey having somewhat greater resistance than the rabbit, but less than the white rat."

PB 6572. DUPONT DE NEMOURS AND CO., INC., E.I. Report on corneal cloudiness from dimethyl diglycolate and related compounds to October 1, 1942. (OSRD Rept. 1015.) November, 1942. 10 pp. Price: Microfilm, 50c.; Photostat, $1.00.

This report from the Ammonia Department describes the results of examining some 31 compounds related to dimethyl diglycolate by the methods previously used in examining dimethyl diglycolate. It is concluded that greater volatility is not an important property of eye-fogging agents, but that what is really needed is a material which will react more rapidly in the eye. Figures 3 and 4 are photographs showing the normal and fogged eyes of a guinea-pig. This work apparently was done with a view to use as a chemical warfare agent, inducing temporary, partial blindness.

PB 19285. EARLY, ROBERT L., AND MORGAN, HERBERT R. The chemotherapy of experimental psittacosis infection (strain 6BC) in mice. May, 1946. 1 p. Price: Microfilm, 50c.; Photostat, $1.00.

This report is an abstract of a paper submitted for presentation at the Society of American Bacteriologists meeting in May, 1946. Sodium sulphadiazine and penicillin were found to be effective agents in the treatment of experimental psittacosis infection in mice when infected by the intravenous or intraperitoneal routes; when the intracerebral or respiratory routes of infection were used the results obtained with sulphadiazine were superior to those detailed with penicillin. Streptomycin had no significant effect.

PB 19280. EIGELSBACH, HENRY T., *et alii*. Electron microscopy of *Bacterium tularense*. May to September, 1945. 1 p. Price: Microfilm, 50c.; Photostat, $1.00.

This report appears to be an abstract of a paper on this subject. "The morphology of *Bacterium tularense* as determined with the electron microscope is in agreement with a recent systematic study of the morphology of this organism by means of vital staining techniques and dark field examination."

PB 19281. ENGLEY, F. B., JUNIOR, AND SNYDER, T. L. Plating media requirements for certain strains of *Bacterium tularense*. No date. 3 pp. Price: Microfilm, 50c.; Photostat, $1.00.

This report appears to be an abstract on this subject. "An extensive survey was made of plating media requirements for *Bacterium tularense* strain Schu. The basal medium consisted of Difco Bacto-peptone, sodium chloride, cysteine, and glucose. This medium was altered in various ways and the results were evaluated on the basis of rate of colonial growth and the variability among counts of replicate plates."

PB 19296. FORGACS, JOSEPH, *et alii*. Studies on streptomycin: I. Assay in body fluids. December, 1944, to October, 1945. 21 pp. Price: Microfilm, 50c.; Photostat, $2.00.

This is a copy of a manuscript prepared for submission to *The Journal of Laboratory and Clinical Medicine*. A method is described for assaying streptomycin in body fluids, particularly blood and urine. This method was developed for investigating the absorption, excretion and activity of the drug in humans and in laboratory animals, and it appears to be accurate and convenient for assaying numerous samples. The results of the procedure are based on the relationship between the diameter of the zone of inhibition and the amount of streptomycin diffusing into an agar plate seeded with a sensitive strain of *Bacillus subtilis* Cohn, *emend* Prasmowski. A method for the quantitative determination of streptomycin and other antibiotics in body fluids has been described in detail. Bibliography, table, photomicrographs and graphs are attached. See PB 19297 below for paper II.

PB 19283. GERHARDT, PHILIPP, AND GEE, LYNN L. Aeration in the cultivation of *Brucella suis*. No date. 2 pp. Price: Microfilm, 50c.; Photostat, $1.00.

This report appears to be an abstract of a paper on this subject. "The aeration requirements of *Brucella suis* in broth culture have been studied with a view to maximum production of cells in a minimum growth period."

PB 19294. HAYWARD, A. E., *et alii*. Strain variation as a factor in the sporulation properties of *Bacillus globigii*. May to June, 1945. 7 pp. Price: Microfilm, 50c.; Photostat, $1.00.

It is shown that variant strains of *Bacillus globigii* possess varying degrees of ability to sporulate under similar environmental conditions. Positive correlation between colonial morphology and sporulating ability is shown for *Bacillus globigii*. The importance of using a pure and stable strain of an organism is indicated for studies on physiological factors affecting endospore formation. Favourable evidence is presented for the use of agitation as an aeration procedure, and a brief description is given of a machine designed for this purpose.

FB 6276. JARMAN, G. N. Vesicant tests on man of pure, thiodiglycol and levinstein mustards in the vapour phase. Unevaporated and 25% evaporated samples. (Edgewood Arsenal Tech. Rept. 79.) September, 1932. 34 pp. Price: Microfilm, 50c.; Photostat, $3.00.

This work describes tests of the comparative vesicant action of the vapour of the two mustards (diglycol and levinstein) using pure mustard as a control. Enclosed are tables, diagrams and graphs.

PB 19297. KORNEGAY, GREAY B., *et alii*. Studies on streptomycin: II. Blood levels and urinary excretion in man and animals. December, 1944, to October, 1945. 28 pp. Price: Microfilm, 50c.; Photostat, $2.00.

This is a copy of a manuscript prepared for submission to *The Journal of Laboratory and Clinical Medicine*. Streptomycin was administered by subcutaneous, intravenous, intradermal, intramuscular, and intraperitoneal injection to the mouse, guinea-pig, rabbit and man, and the blood levels of the drug determined at various intervals after administration. Maximum blood levels appeared from fifteen to sixty minutes following its injection. Administration of streptomycin apparently does not affect the count of red or white blood cells. See PB 19296 above for paper I.

PB 19278. MILLER, EDWARD S., *et alii*. Chemotherapy of experimental anthrax infections. February-August, 1945. 22 pp. Price: Microfilm, 50c.; Photostat, $2.00.

The investigations reported represent an attempt to evaluate the efficacy of sulphadiazine, penicillin and streptomycin in experimental anthrax infections in mice. Tables, graphs and bibliography are attached to the report. Maximum survival rates of 92% were obtained with streptomycin, 58% with penicillin and only 5% with sulphadiazine.

PB 19292. O'KANE, D. J. The substitution of thiamin for the heat and alkali labile fraction of red blood cell extract in the growth of *Bacterium tularense*. March-July, 1945. 3 pp. Price: Microfilm, 50c.; Photostat, $1.00.

It has been found that the activity of the red blood cell extract required for the growth of *Bacterium tularense* is destroyed by heating at 120° C. for one hour in 0·08 N NaOH, but not by similar treatment with 0·08 N HCl. The activity removed by the alkali treatment may be completely restored by the addition of thiamin.

PB 6285. REZNIKOFF, PAUL. Micrurgical studies of the action of bis (β-hydroxyethyl) ether, bis (β-chloroethyl) ether, bis (β-chloropropyl) sulphide, bis (β-aminoethyl) sulphide, and bis (β-diethylaminoethyl) sulphide on *Amœba dubia*. (Edgewood Arsenal Tech. Rept. 16.) March, 1931. 32 pp. Price: Microfilm, 50c.; Photostat, $3.00.

An investigation of the relation between toxicity and structure by micrurgical studies of the physiological action of certain compounds, closely related to mustard gas, on *Amœba dubia*. Attached is an addendum by E. S. Linthicum.

British Medical Association News.

SCIENTIFIC.

A MEETING of the South Australian Branch of the British Medical Association was held on August 29, 1946, at the Verco Theatre, Institute of Medical and Veterinary Science, Adelaide; Dr. L. R. MALLEN, the President, was in the chair at the beginning of the meeting, and DR. JOHN MAYO took the chair later. The meeting took the form of a number of ten-minute talks and demonstrations by members of the Radiological Section of the Branch. Part of this report appeared in the issue of December 14, 1946.

X-Ray Films Illustrating Chest Conditions.

DR. J. S. VERCO showed a series of films which, he said, all showed similar appearances, although there were differences which were not strikingly apparent. Dr. Verco admitted that some films taken at other stages of disease made the differentiation more apparent. He said that the films were shown with the object of emphasizing the necessity for having as many as possible of the relevant clinical facts made available to the radiologist, so that a more helpful interpretation might be given of the X-ray evidence. The conditions demonstrated were silicosis, pulmonary tuberculosis, sarcoidosis and miliary tuberculosis.

Dr. Verco said that the patient suffering from silicosis was found on preemployment medical examination. Several years before he had worked as an underground miner, and at the time of the meeting had slight dyspnœa on exertion.

The patient suffering from pulmonary tuberculosis was found on examination prior to discharge from the armed forces. He felt well, and had no fever, cough or dyspnœa. The Mantoux test produced a positive reaction. Examination of the sputum for tubercle bacilli gave positive findings on four occasions.

The patient suffering from sarcoidosis had been referred by the dermatologist on account of the skin condition. There were no signs or symptoms referable to the chest.

The patient suffering from miliary tuberculosis had recently undergone an operation for an advanced tuberculous condition of the kidney; this had been followed by pyrexia, cough, dyspnœa and cyanosis.

Transitional Cell Epidermoid Carcinoma of the Tonsil.

DR. JOHN MAYO discussed a case of transitional cell epidermoid carcinoma of the tonsil. Dr. Mayo said that the case he was reporting was of interest because it differed in certain respects from the more usual squamous-cell epithelioma of the tonsil. He thought that the condition had first been described under its present name by Quick and Cutler in about 1927, and although it was regarded as rather rare and had seldom been reported in South Australia, these authors stated that 10% of cancers of the tonsil and of the base of the tongue were of this type and were often incorrectly recorded as endothelioma or lymphosarcoma. These authors also stated that the cells were small and uniform in size, with large hyperchromatic nuclei and scanty cytoplasm. Adult squamous characters were absent. The condition appeared to be an anaplastic undifferentiated epithelioma. Dissemination was apt to be wide and early, and the primary tumour, which was often small, might pass unnoticed. The tumour was radio-sensitive, and because of the danger of dissemination, it was desirable to avoid trauma in its treatment.

Dr. Mayo went on to say that the patient, a man, aged forty-five years, contracted mumps in about November, 1945. During the attack he noticed and complained of dryness of the right side of the throat. This did not abate and the tonsil ulcerated, giving rise to a blood-stained discharge. He was first regarded as suffering from Vincent's angina and was given penicillin lozenges to suck, without improvement. He was subsequently referred to Dr. Sydney Cocks, who took a biopsy specimen; examination revealed transitional cell epidermoid carcinoma.

Dr. Mayo first examined the patient four months after he had first complained of his throat condition. The right tonsil was then ulcerated, a mass was palpable above it behind the soft palate, and the growth had produced a perforating ulcer of the soft palate. A blood-stained discharge was still present. No glands were clearly palpable. He was treated with deep X-ray therapy, three external fields and subsequently an intraoral field being used. A tumour dose of 4,500*r* given in just over three weeks was administered by means of the external fields, and a fortnight later 1,100*r* were given by the intraoral route. A brisk reaction followed, with epilation of the skin fields. The ulcerated areas healed rapidly and the mass disappeared. He had not undergone a dissection of the glands. He had gained considerably in weight, and showed no sign of recurrence. On examination some slight scarring could be seen; all other abnormality had disappeared.

Dr. Mayo said that the case was not put forward as a cure, if that debated word could be employed, as treatment had been too recent. However, several points of interest emerged: (i) the relative youth of the patient, compared to the age of patients with the more usual squamous type of growth; (ii) the fact that he had never smoked—this was most unusual; (iii) the ready response to irradiation.

Dr. Mayo went on to say that for purposes of comparison he proposed to make a brief mention of other cancers of the tonsil. They comprised (i) epidermoid carcinoma or squamous-cell epithelioma, (ii) lympho-epithelioma, (iii) lymphosarcoma. The first was the commonest and occurred in the elderly. Thus 60% of a five-year group of patients at the Royal Adelaide Hospital were aged over seventy years; almost all were smokers, syphilis appeared to play no part and most of the patients were males. Dr. Mayo said that in the time at his disposal he could do no more than stress the fact that treatment was or should be by irradiation.

At the radiotherapy clinic at the Royal Adelaide Hospital during the years 1929 to 1945, 46 patients with epidermoid carcinoma or squamous-cell epithelioma of the tonsil were treated. Sixteen died in the first year after treatment, fourteen in the second year, six in the third year, one in the fourth year, and two in the fifth year; two were untraced. One was dead of metastases after more than five years, the tonsil remaining healthy. Three were alive and well or had died of other causes more than five years after treatment. One was alive and well less than five years after treatment. Three had died of other causes less than five but more than three years after treatment. The total salvage might therefore be regarded as about 15%. The types of treatment given are set out in Table I.

Dr. Mayo said that the results were poor, but it had to be remembered that in many cases the condition was

TABLE I.

Mode of Treatment.	Number of Patients.	Died. (Years after Treatment.)					Untraced.	Well.	Died More than Five Years After.
		1	2	3	4	5			
Deep X rays	19	7	9	1			2		
Radium needles and collar ..	6	2	1	3					
Radium needles and deep X rays	6	3	1	1	(1)[1]				
Radium needles	5	3	1					1	
Diathermy and deep X rays ..	4	1	1	1		(1)			
Diathermy and radium needles	2		1						(1)
Radium needles and collar and deep X rays	1								1
Radium needles and block dissection	1								(1)
Deep X rays and block dissection	1					(1)			
Deep X rays and tonsillectomy	1							1	
Totals	46	16	14	6	1	2	2	2	3

[1] Figures in parentheses indicate patients who died of other disease and without apparent recurrence more than three years after treatment.

advanced when the patient was first examined; large and fixed glands were present, and some patients were barely able to open their mouths. The most severely affected were treated with deep X-ray therapy alone, and some of them received dosage that would probably now be regarded as insufficient. In other parts of the world better results had been obtained with the use of the radium bomb or with concentrated deep X-ray therapy. It was hoped that with more intensive treatment the results in Adelaide also might be improved. One important aid would be the earlier diagnosis of such cases.

Dr. Mayo then said that lymphoepithelioma was another rare growth affecting chiefly the base of the tongue, the tonsil and the naso-pharynx. The tumour was often small and did not ulcerate early. However, wide and early metastases were apt to occur. The tumour was radiosensitive. No case had been recorded at the Royal Adelaide Hospital; but at the time of the meeting there was a patient who had just been treated for widespread involvement of the glands of the neck; he might well be suffering from the disease. In his case no primary tumour had yet been found.

Dr. Mayo said that lymphosarcoma was another growth that might occur primarily in the tonsil. One patient with this type of growth had been treated at the clinic, with apparent success. A patient treated in his private practice survived for nine years, but eventually died of the disease. Lymphosarcoma also was radio-sensitive.

Dr. Mayo then referred briefly to other types of tonsillar growth treated at the Royal Adelaide Hospital. He said that in 1934, on examination of a section from a tonsil, the pathologist described the condition as either diffuse epithelioma or endothelial tumour; the patient was treated with deep X rays, and died nine years later of cerebral hæmorrhage. In 1942 a case was recorded of lymphosarcoma, apparently limited to one tonsil. The patient was treated by tonsillectomy and deep X rays, and remained well in 1946. In 1944 there was a case of endothelial sarcoma of the right tonsil. The patient was treated by the application of a massive radium mould, dissection of a metastatic gland, interstitial insertion of radium, and deep X rays. In 1946 she was still alive, her general condition was good and she was in no discomfort; but a residuum of the growth was still present. The patient was a young woman, aged about thirty-five years.

In conclusion, Dr. Mayo reiterated the belief that the treatment of this group of diseases was primarily by irradiation. He also thanked Dr. F. S. Hone, Honorary Director of the Radiotherapy Clinic at the Royal Adelaide Hospital, for permission to include data from that source.

DR. F. S. HONE pointed out the similarity between epithelioma of the tonsil and branchiogenic cyst carcinoma.

The Use of Lipiodol.

DR. H. A. McCOY showed a series of films illustrating cases in which the maxillary antra had been injected with lipiodol. The films were selected from a group of cases in which Dr. R. M. Glynn had injected the antra, when a plain X-ray film of the paranasal sinuses had indicated the likelihood of pathological change in one or both antra. The group was confined to those cases in which the symptoms suggested chronic disease, but it excluded cases in which symptoms and clinical signs made the diagnosis of gross disease obvious, and it excluded also cases in which the upper respiratory symptoms were acute.

Dr. McCoy said that in the light of this experience Dr. Glynn considered that it was not justifiable to open an antrum without first obtaining the added evidence available in the X-ray film of the antrum injected with lipiodol. The conditions illustrated in this demonstration were designed to show four different conditions. The first was normal mucosal lining, in cases in which plain X-ray films of the antra revealed an opacity that gave rise to suspicion of organic change. Conditions which might give rise to these confusing appearances were considered—namely, (*a*) the size of the antral cavity, (*b*) the thickness of the bone wall, (*c*) the inclination of the bone wall, (*d*) the bony septa, (*e*) allergic conditions. Mucosal thickening was demonstrated in three cases, in which the evidence of pathological change indicated on the plain film was confirmed. Gross mucosal thickening in the antral cavities was illustrated. In these cases only small droplets of lipiodol could be introduced into the very contracted cavity. Polyposis, it appeared, might be demonstrated more effectively in those cases in which lipiodol was injected into the antra.

Dr. McCoy said that the cases illustrated dealt only with the common conditions met with in the maxillary antra, and were designed only to illustrate, in a short contribution, the value of the method, and to admit freely the abundant imperfections of the technique so far developed.

DR. R. M. GLYNN said that he had been associated with Dr. McCoy in the work on injection of lipiodol into the maxillary antrum. The procedure was necessary in the full investigation of suspected antral disease. A plain X-ray film was not sufficient as the sole justification for operation, and in doubtful cases lipiodol should be used.

Ewing's Sarcoma.

DR. COLIN GURNER discussed a case of Ewing's sarcoma. He said that he was presenting the case to illustrate the difficulty in making a diagnosis, both clinically and radiologically, in certain bone conditions, and to emphasize the importance of making the correct diagnosis as early as possible. Early diagnosis and treatment were essential in all malignant bone lesions. Even so, the prognosis was extremely grave, and a large percentage of cases terminated fatally.

The patient, a male, aged nineteen years, was admitted to hospital on July 17, 1946. Three months prior to his admission to hospital he had noticed a shooting pain in the outer side of the right thigh, which lasted for about two days. One month later the pain recurred, and on the following day it was severe, but it subsided two or three days later. After that the pain recurred periodically, and tended to disappear during the day, returning in the early morning. The patient had been walking with a limp for this period, and sometimes had a shivering attack on retiring, with occasional night sweats. He had lost one stone in weight.

On examination on July 17 the patient was a thin, wasted lad, looking ill. Some fullness was present in the right thigh below the greater trochanter, with tenderness on the inner side high up and in the femoral triangle. All movements were painful, but not extremely so. His temperature on his admission to hospital was 100° F., and it rose to 104° F. a few hours later. The hæmoglobin value of his blood was 72%, and the leucocytes numbered 21,000 per cubic millimetre. The blood was sterile.

The leg was immobilized on pillows and a course of penicillin and sulphamerazine was started. X-ray examination on July 17 revealed periosteal new bone extending from the lesser trochanter down the medial side of the shaft. This new bone was laminated and slightly elevated. Periosteal new bone was also present on the outer aspect of the femur extending from the greater trochanter for about six inches downwards. The lower portion of this was irregular and had an abrupt upper margin, and there was no lamination on this side. The cortex showed no erosion, but a little indefinite rarefaction was present. On July 22 the leucocytes numbered 8,900 per cubic millimetre. The temperature came down on July 19, 1946, and remained about normal until July 23.

The clinical evidence at this stage, with the high temperature, leucocytosis and pain, followed by a fall in temperature and a normal leucocyte count after penicillin and sulphamerazine therapy, favoured a diagnosis of an inflammatory bone lesion. This was somewhat supported by the X-ray changes, though certain of these were more typical of neoplasm. However, as the diagnosis was still in doubt, on July 23 an exploratory operation was performed. An incision was made below the greater trochanter, and a creamy fluid, thought to be pus, was obtained. A biopsy specimen was removed for immediate examination. No organisms could be grown from the pus, and few pus cells were found. The report on the biopsy specimen was: "Ewing's sarcoma with areas of inflammation and fibrosis." Owing to the site and probable extent of the lesion, amputation was contraindicated, so deep X-ray therapy was started as soon as possible. On July 27 the patient complained of pain in the left leg, but subsequent X-ray films revealed no metastases, though there was further deposition of new bone at the site of the lesion. Transfusions were given on several occasions, and after operation the temperature rose to 102° F. or higher nearly every day. At the time of the meeting a course of deep X-ray therapy had almost been completed, but it was too early to determine the effect. However, the patient's condition was not so good as to warrant optimism.

Dr. Gurner then discussed Geschickter and Copeland's description of Ewing's sarcoma; these authors had collected 54 cases. The disease was said to be one of early life, and 95% of their patients were aged between four and a half and twenty-five years. A history of trauma was not uncommon. Pain was usually the first symptom, beginning spontaneously after trauma, or appearing simultaneously with the formation of a tumour. Pain was usually intermittent, lasting from a few hours to several days, only to recur with increasing severity. Nocturnal pain was the most severe. A tumour could be palpated in 90% of their cases. In 19% a tumour was the initial finding. The site

of election was in the shaft of the long bones, often near the middle. Pathological fracture was rare. The temperature varied from 99° to 104° F. Pyrexia was more commonly found in the later stages and in the presence of metastases. Mild secondary anæmia was usually present. Leucocytosis was generally present, often up to 20,000 per cubic millimetre; it might occur early and was not restricted to patients with metastases. Loss of weight was often pronounced, with progressive emaciation in the terminal stages. With regard to X-ray changes, it was stated that the first changes were periosteal with new bone formation, often laminated—the so-called "onion peel". The periosteum became separated from the cortex, and the tumour was largely subperiosteal, tending to infiltrate rather than to destroy bone, except in the later stages. In the early stages there was little evidence of medullary involvement, though later rarefaction and cortical erosion were present. New bone might be laid down in spicules perpendicular to the cortex in the later stages. The epiphysis was only rarely involved, and then secondarily. Metastases were most frequently seen in the lungs, lymph nodes and skull. However, metastases might occur in all the bones of the skeleton, and often so rapidly as to suggest multiple primary lesions. In the differential diagnosis the following conditions might be mistaken for Ewing's sarcoma: (i) pyogenic periostitis and osteomyelitis, especially subacute or chronic; "these conditions after penicillin or sulpha drug treatment may be extremely difficult to differentiate radiologically"; (ii) bone tuberculosis, mainly on clinical grounds; (iii) syphilitic periostitis; (iv) osteogenic sarcoma, which generally occurred in the ends of the long bones; new bone was more often formed at right angles to the cortex and not laminated; the osteolytic type caused gross destruction with little or no new bone; (v) metastatic carcinoma, in which bone destruction only was usual.

Dr. Gurner went on to say that in Geschickter and Copeland's series of 54 cases the mortality rate was 87%. The average duration of symptoms at the time of operation was above twelve months. The average pre-operative duration of symptoms of the surviving patients was twenty months, as against six months for those who died within one year. The short duration of symptoms suggested a more rapidly growing tumour and a more grave prognosis. The post-operative duration of life averaged sixteen months in the fatal cases. In cases in which there was no evidence of metastases, for lesions of the lower extremity below the upper third, amputation was performed, and resection of bones was performed for lesions in the upper extremity following pre-operative irradiation. Ewing's sarcoma was more radio-sensitive than most other malignant bone lesions. For extensive lesions, when operation was not considered justifiable, deep X-ray treatment was given. There were eight survivals five years after treatment; three of these patients had amputations or resection with irradiation, four had amputations or resection alone, and one had irradiation alone following exploratory operation. In conclusion, Dr. Gurner expressed his thanks to Dr. I. B. Jose for permission to use the case notes and X-ray films of his patient.

Angioma in Young Children.

DR. C. SMEATON showed a series of patients, with the permission of the honorary dermatologist of the Adelaide Children's Hospital, to demonstrate the results of X-ray treatment of large angiomata in young children. Dr. Smeaton emphasized two points: (i) that nævi should be treated as early as possible, when they were most sensitive to irradiation; (ii) that the minimum amount of irradiation should be given, to avoid atrophic scarring in later years. He said that a very small dose of radiation would start the obliteration of the vessels, and no scarring should follow. The lesions in the cases under discussion were extensive, involving the whole of the forearm or the leg. The skin was thin and in some areas ulcerated. Extensive ulceration and infection resulted from small doses of X rays, and cod liver oil ointment was used. At the present time much more rapid results would be obtained with penicillin ointment. X-ray examination of the bones revealed negligible shortening of the limb treated with superficial irradiation. Deep X rays used in another case of a large nævus of the lateral abdominal wall caused a decrease in size of that side of the body. Dr. Smeaton said that the results five years after treatment were satisfactory; function of the limbs was full, and there was little scarring of the skin.

The first patient shown by Dr. Smeaton had been born with a cavernous angioma on the back of his left knee. He was treated from February 29, 1940, when aged between one and two months. On that date, to a field measuring 4·0 inches by 2·5 inches, 1,000*r* were given over twenty minutes with the following factors: four milliamperes, 100 kilovolts, a filter of one millimetre of aluminium and a field skin distance of 12 inches. A reaction was present on May 20, and on June 18 the area affected by the reaction had a central slough. On May 7, 1940, a further dose of 700*r* was given to the right and left sides of the leg; the size of each field was 3·5 inches by 2·0 inches.

Dr. Smeaton's second patient was a male, aged eleven months, who had an angioma on his left forearm. On December 20, 1940, the whole forearm was treated; a dose of 840*r* was given, 420*r* to each side. On January 3, 1941, a blistering reaction with erythema was present. On February 7 infection of the skin was present, with sloughing mainly in the folds. By February 28, 1941, the condition was healed.

Dr. Smeaton finally showed a female patient who had been treated from the age of nine months for an angioma on the right forearm. On August 31, 1942, a dose of 200*r* was given to the dorsal aspect of the forearm, and on November 2, 1942, 200*r* were given to the palmar aspect. On January 6, 1943, 200*r* were given to the dorsal aspect and 200*r* to the palmar aspect. On March 24 the lesion was breaking down in folds; healing was achieved with cod liver oil ointment. On July 5 and September 13, 1943, doses of 200*r* were given to the upper palmar aspect of the forearm. On November 8, 200*r* were given to the lower palmar aspect, and on January 10, 1944, a dose of 200*r* was given to the upper palmar aspect of the forearm.

Conclusion.

Dr. J. C. Mayo, on behalf of the Australian and New Zealand Association of Radiologists, thanked the Council of the South Australian Branch of the British Medical Association for the opportunity to conduct the meeting.

Dr. Mallen, from the chair, thanked those who had read papers and those who had contributed to the discussion.

Correspondence.

THIOURACIL AND HYPERTHYREOIDISM.

SIR: In connexion with the claims being made for certain derivatives of 2-thiouracil (for use in thyreotoxicosis) it is perhaps worth while to draw attention to the conclusions obtained by E. B. Astwood[1] with respect to the use of 6-n-propyl thiouracil, as this drug does not appear to have received the attention it merits. He concluded that both the 6-ethyl and 6-n-propyl derivatives were five times as active as thiouracil itself. From animal experiments he decided that the 6-n-propyl derivative had superior anti-thyreoid potency to the 6-ethyl compound and had a more prolonged action following a single dose. It was estimated that 25 milligrammes of propyl-thiouracil at eight or twelve hour intervals was an adequate dose to restore metabolic equilibrium and that this state could be maintained by a daily dose of from 25 to 50 milligrammes in the human being. He reported no side effects in a total of 52 individuals receiving the drug in therapeutic dosages.

Yours, etc.,

L. E. A. WRIGHT.

Kanematsu Memorial Institute of Pathology,
Sydney Hospital,
Sydney.
December 9, 1946.

THE TREATMENT OF THYREOTOXICOSIS BY CONCURRENT ADMINISTRATION OF THIOURACIL AND IODINE.

SIR: The article under the above heading by Maxwell, Gunter and Schwartz which appeared in THE MEDICAL JOURNAL OF AUSTRALIA, December 7, 1946, was of particular interest as regards the medical treatment of thyreotoxicosis. Of their 56 patients, subtotal thyreoidectomy was performed on nineteen with one death due to acceptance of a risk under unusual circumstances, an occurrence which happens occasionally to all surgeons dealing with toxic goitres and one which I experienced recently after a clear run of four years. There is general agreement that the use of iodine is advisable for all patients treated with thiouracil who are to be subjected to operation, but most authorities administer it for two or three weeks prior to operation and after the

[1] E. B. Astwood and W. P. Vanderlaan: "Thiouracil Derivatives of Greater Activity for the Treatment of Hyperthyroidism", *The Journal of Clinical Endocrinology*, Volume V, December, 1945, page 424.

thyreotoxicosis has been controlled with thiouracil. On page 790 of the same issue of the journal, mention is made as to how Spencer and I came to use iodine in these cases before it was reported from the Lahey Clinic. No mention is made by Maxwell, Gunter and Schwartz as to how long was taken in the preparation of patients for operation, but one may deduce from Figure IV that it was some twenty to thirty days, that is, approximately double the average time for iodine preparation alone. If this is so, was the concurrent use of thiouracil justified, and especially since all patients were confined to bed during their pre-operative treatment? One's own personal experience is that control of thyreotoxicosis can now be secured with thiouracil with the patient ambulatory in most cases; then iodine is commenced before the patient enters hospital, so that only five to seven days are required in bed prior to operation, a matter of great economic importance, especially to the basic wage earner.

One is in full agreement with the "selection of patients for thyreoid resection" mentioned by these joint authors, and their support in advocating operation for patients with nodular (adenomatous) goitres is welcome. Of particular interest was their Table I, being a chart of patients treated with thiouracil and iodine without surgery—37 in all—but it is noted that two were referred for operation; of the remaining 35, only six were treated as ambulatory with results listed as "very good" and "excellent", although one patient after eight months' treatment had a basal metabolic rate of +24% and the average time of treatment was nine and a half months with five patients still continuing treatment. It is interesting to compare this with one's results in the treatment of 38 patients with methyl thiouracil when the average duration of treatment was six and a half months with apparent control of the thyreotoxicosis and normal basal metabolic rate persisting for two to six months after cessation of all treatment.

As far as can be seen in these 35 cases under discussion, only five patients are listed as having ceased treatment for more than four months, and of these three had basal metabolic rates of +14%, +10% and +31% after treatment; and in the series thirteen patients have basal metabolic rates of over 10%, yet the results are classed as fair, good, very good or excellent. In my own practice a basal metabolic rate of +10% is regarded as evidence of persisting thyreotoxicity, and I am not satisfied unless the final result is +5% or less over a minimum period of three to six months. Also it is noticed that fifteen of the patients listed have had under five months' treatment, this period of time being regarded by me as the minimal period before treatment can be stopped and any evaluation of the final result made.

The fact of major importance in the use of the thio compounds is that at last we do seem to have a form of treatment, which, intelligently used in the right sort of case, may give a cure in acute thyreotoxicosis without resort to surgery. The "right sort of case" falls into four groups: (1) the typical Graves's disease with acute onset and the even hyperplastic gland, (2) the acute thyreotoxicosis of middle life with the evenly enlarged gland, and (3) the *"forme frustre"* type in later life with no visible or palpable enlargement of the thyreoid gland, (4) recurrent thyreotoxicosis after operation or deep X-ray therapy. It is to be noted that these are all cases of primary acute thyreotoxicosis, except the recurrent cases, as all secondary types of thyreotoxicosis should be submitted to operation.

In view of the results published by Spencer and myself in the journal, April 13, 1946, and of my own series with methyl thiouracil in the journal, December 7, 1946, it does not seem that coincident administration of iodine with thiouracil can give anything comparable either as final results or as to the time taken to secure the results. We tried this method in some of our earlier cases, but abandoned it. When one sees that (*a*) four of the thirty-five patients listed were under treatment from 23 to 26 months, (*b*) two of them had final basal metabolic rates of +10% with one of them still continuing treatment, (*c*) nine others were treated for ten to nineteen months, five of whom were still continuing treatment, it makes one wonder why this combined therapy has been persisted with.

As pointed out, with methyl thiouracil the average time for an adequate response to a zero or *minus* metabolism by 25 patients who received no iodine before treatment was four and a half weeks, whereas in thirteen cases in which the patients were previously treated with iodine it took nine weeks, with an average drop in both cases of 32% in the basal metabolic rate. This lag period in response to thiouracil in cases in which iodine therapy has been used has been commented on by most writers. As regards the drop in pulse rate and metabolism when the patient is put to bed under sedation, this was established many years ago, but nowadays when the majority of these patients can be treated as ambulatory and without their ceasing work, it is the active and not the resting metabolic rate that counts. The sections of glands before and after treatment confirm the results obtained years ago under the old iodine preparation, but so far no distinguishing histological change has been found in the gland treated by thiouracil when removed at operation, although all workers have been keenly searching for some constant demonstrable effect.

Among the 37 patients mentioned in Table I, two developed agranulocytosis, that is, over 5%, which is a high figure as compared to one's own which is now only 0·5%; two developed pyrexia; one showed thiouracil sensitivity (unspecified) and was operated upon; two abandoned the treatment; in one case thiouracil was discontinued as exophthalmos developed during the course of treatment; and in nine cases joint and muscle pains and swellings occurred. In a small series of cases this is a formidable list of toxic symptoms directly attributable to thiouracil, and the only explanation that can be given is that incorrect dosage has been employed and adjuvant therapy has been neglected. If *Thyroideum Siccum* had been given in the case in which exophthalmos developed this condition could have been controlled.

I would draw particular attention to the conclusions arrived at and mentioned by me in the article on methyl thiouracil appearing in the journal, December 7, 1946, page 800.

In conclusion, thanks should be extended to the authors for publishing the results of a very interesting experiment in the coincident administration of thiouracil and iodine, which on theoretical grounds seemed promising.

Yours, etc.,

225, Macquarie Street, HUGH R. G. POATE.
Sydney,
December 12, 1946.

THE DEVELOPMENT OF CLINICAL PATHOLOGY.

SIR: In a very interesting article in your issue of December 14, 1946, page 830, Dr. Lucy M. Bryce places her first stage, when most hospitals of standing were beginning to appoint pathologists to their staffs, in the era just prior to World War I.

Sydney Hospital must then have been well in the forefront, for in the last years of last century Dr. Sydney Jamieson, "a consultant physician who had a liking for laboratory work", was Director of the Pathological Department, and he or his resident assistant undertook blood examinations, microscopical and cultural examination of sputum, urine *et cetera*, histological biopsy of tumours, tests for sterility of hands of operating theatre staffs and germ content of theatre air.

Yours, etc.,

GUY GRIFFITHS, M.D., F.R.A.C.P.
Sydney,
December 13, 1946.

GELATIN INJECTION IN MAN.

SIR: In your issue of November 30, page 781, there is an abstract of an article on gelatin injection in man which appeared in *The Journal of Clinical Investigation*. May I sound a note of warning? When Bayliss was searching for something to add to physiological saline which would make its viscosity equal to that of blood and at the same time introduce a colloid which would balance the colloids of tissue cells, he naturally thought of gelatin. But it so happened that at the time of the research strong gelatin solution had been injected into a sessile aneurysm in the hope that the gelatin when set would stop ballooning of the aneurysm wall. Unfortunately the patient died of tetanus, and subsequent inquiry showed that much gelatin on the English market had been derived from animals, chiefly horses in China, which had died of tetanus. Bayliss then tried effective sterilization of gelatin, but found that sufficiently long boiling or heating under pressure to obviate all possibility of tetanus infection so lowered the viscosity and colloidality that the gelatin thus treated was useless for his purpose. So reluctantly he fell back on gum acacia.

Yours, etc.,

The Hall, W. A. OSBORNE.
Kangaroo Ground,
Victoria.
December 13, 1946.

"RADIOLOGIST" AND "RADIOGRAPHER".

SIR: At a recent Council meeting of this Association, attention was drawn to the meaning of the words "radiologist" and "radiographer".

By common usage the word "radiologist" is now only used as applying to a medical man specializing in the practice of medical radiology. The word "radiographer" is applied to those technicians working in X-ray and radium laboratories and associated in the management thereof and who are trained in the technique.

The Fellowship of the Faculty of Radiologists, London, is now considered to be the highest post-graduate radiological diploma. The Association of Radiographers, which is registered under the British Government, requires the technicians to obtain the certificate before they can be admitted to this Association.

Yours, etc.,
A. T. NISBET,
President.

Australian and New Zealand Association of Radiologists,
Macquarie Street,
Sydney.
December 16, 1946.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 233, of December 12, 1946.

CITIZEN NAVAL FORCES OF THE COMMONWEALTH.

Royal Australian Naval Reserve.

The appointments of the following officers have been terminated:

Surgeon Lieutenant-Commander Nicholas Larkins, 31st January, 1946.

Acting Surgeon Lieutenant-Commanders Hamilton D'Arcy Sutherland, 11th December, 1945, Graeme Lindsay Grove, 13th June, 1946, and Keith Campbell Bradley, 25th September, 1946.

Surgeon Lieutenants (Acting Surgeon Lieutenant-Commanders) Richard Fitzwalter Read, 14th September, 1945, and Sydney Ralph Reader, 13th March, 1946.

Surgeon Lieutenants William Dinwoodie Ackland-Horman, 19th April, 1945, Kenneth Newman Morris, 30th October, 1945, Gordon David Ley, 15th February, 1946, Colin Keith Hambly, 17th September, 1946, Ian Campbell Galbraith, 19th February, 1946, John Russell Robert Taylor, 27th February, 1946, Ronald Mackenzie Macintosh, M.B.E., 6th September, 1946, Franklin Robert Fay, 12th September, 1946, Michael Dean Dawson, 18th September, 1946, John Lawrence Bignell, 19th September, 1946, Victor Macky Hercus, 2nd October, 1946, Marcus Gordon Jansen, 25th October, 1946, Bruce Lambton Menzies, 25th October, 1946, Max Kimberley Anderson, 25th October, 1946, Charles William Wilson, 25th October, 1946, and Graeme Larkins, 25th October, 1946.

Royal Australian Naval Volunteer Reserve.

The appointments of the following officers have been terminated: Surgeon Lieutenants Ewen Garth McQueen, 20th November, 1945, Noel Walter Bartrop, 18th February, 1946, Wilfrid Lievesley Nickson, 25th October, 1946, William Henry Roberts, 25th October, 1946, Robert Samuel Irwin, 25th October, 1946, William Walter Seed, 28th October, 1946, and Bernard Balfour Garrett, 28th October, 1946.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Hicks, Kenneth Edward, provisional registration, 1946 (Univ. Sydney), Maitland Hospital, West Maitland.

Harris, Louis Leslie, M.B., B.S., 1940 (Univ. Sydney), 268, Victoria Avenue, Chatswood.

The undermentioned have been elected as members of the South Australian Branch of the British Medical Association:

Cheesman, Graham Frank, M.B., B.S., 1946 (Univ. Adelaide), Springbank Road, Clapham.

Fowler, Malcolm Charles, M.B., B.S., 1946 (Univ. Adelaide), 1, Barker Road, Prospect.

Corrigendum.

THE title of a paper by Dr. J. Parkes Findlay in the issue of December 21, 1946, was incorrectly stated. It should be: "Operation for Bell's Palsy by Decompression and Incision of the Sheath of the Facial Nerve."

Diary for the Month.

JAN. 6.—N.S.W. Branch, B.M.A.: Executive and Finance Committee.
JAN. 7.—N.S.W. Branch, B.M.A.: Council Quarterly.
JAN. 21.—N.S.W. Branch, B.M.A.: Medical Politics Committee.
FEB. 4.—N.S.W. Branch, B.M.A.: Organization and Science Committee.
FEB. 4.—N.S.W. Branch, B.M.A.: Special Groups Committee.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Honorary Secretary, 135, Macquarie Street, Sydney): Australian Natives' Association; Ashfield and District United Friendly Societies' Dispensary; Balmain United Friendly Societies' Dispensary; Leichhardt and Petersham United Friendly Societies' Dispensary; Manchester Unity Medical and Dispensing Institute, Oxford Street, Sydney; North Sydney Friendly Societies' Dispensary Limited; People's Prudential Assurance Company Limited; Phœnix Mutual Provident Society.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federated Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225, Wickham Terrace, Brisbane, B.17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178, North Terrace, Adelaide): All Lodge appointments in South Australia; all Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205, Saint George's Terrace, Perth): Wiluna Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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